

**A Comparison of Personality Dimensions and Retrospective Family
functioning in Chronic fatigue syndrome and Depression**

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Declaration

This thesis has been composed by myself and the work contained herein is my own.

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August 2000

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ABSTRACT

The nature and aetiology of chronic fatigue syndrome (CFS) has been the subject of much controversy and debate over recent years and remains poorly understood. A review of the literature available would seem to suggest that it is an aetiologically complex, heterogeneous disorder.

A large number of studies have demonstrated a high degree of psychiatric co-morbidity with CFS and mood disorders have been found to co-occur most commonly. Various hypotheses have been proposed to account for the relationship between CFS and depression, including the following: -

1.) The view of CFS as an atypical manifestation of major depressive disorder (MDD).

Further, it has been proposed that somatisation and alterations in the central and autonomic nervous systems may underlie the somatic expression of psychological symptoms suggested by this hypothesis.

2.) The Depression- Vulnerability Hypothesis proposes that CFS occurs in individuals with a pre-morbid vulnerability to depression and the prolonged disability associated with CFS may be attributable to MDD.

3.) The hypothesis that depression may occur as the result of CFS and may represent a reaction to loss of health or a psychiatric disorder of organic origin.

This study investigated current psychiatric morbidity and the pre-morbid prevalence of psychiatric disorder in a sample of thirty-five patients with CFS. Seventy-one per cent of this sample satisfied criteria for current psychiatric disorder. Fifty-four per cent satisfied criteria for depressive disorder, and a further thirty-seven per cent satisfied criteria for an

anxiety disorder. The pre-morbid prevalence of psychiatric disorder and MDD was forty-two per cent and thirty-one per cent respectively. These results are comparable to those found in previous studies.

Attribution of symptoms by CFS patients to external and internal causes was also investigated and the relationship between attributional style and depressive symptomatology was explored.

The relationship between depression and CFS was further explored by comparison of the CFS sample with a sample of thirty-three patients with major depressive disorder or dysthymia, in terms of subjective fatigue, personality factors and dimensions of family functioning (family of origin). Subjects in the CFS sample with concurrent depression formed a sub-group for the purpose of statistical analysis. The results were subjected to statistical analysis and the findings were then discussed in relation to aetiological theories of CFS and the various hypotheses proposed to explain the relationship between mood disorders and CFS.

1	LITERATURE REVIEW	9
1.1	INTRODUCTION	9
1.2	HISTORY	10
1.3	DEFINITION OF CFS, IDIOPATHIC CHRONIC FATIGUE AND FIBROMYALGIA.....	12
1.3.1	Chronic fatigue syndrome.....	12
1.3.2	Idiopathic Chronic Fatigue	14
1.3.3	Fibromyalgia.....	15
1.4	EPIDEMIOLOGY.....	16
1.5	AETIOLOGY	17
1.5.1	Biological Models	17
1.5.2	Psychiatric/Psychosocial Models	20
1.5.3	Multi- factorial Models and Multiple Aetiologies.....	24
1.6	THE OVERLAP BETWEEN PSYCHIATRIC DISORDER AND CHRONIC FATIGUE SYNDROME	25
1.6.1	Mood Disorders.....	26
1.6.2	Somatisation Disorders.....	29
1.6.3	Personality	31
1.7	THE RELATIONSHIP BETWEEN DEPRESSION AND CHRONIC FATIGUE SYNDROME.....	36
1.7.1	CFS as an atypical manifestation of major depressive disorder	37
1.7.2	The Depression Vulnerability Hypothesis	44
1.7.3	Depression as a result of chronic fatigue syndrome	50
1.7.4	CFS and Major depressive disorder as Covariates	55
1.7.5	MDD as an Artefactual Diagnosis.....	55
1.8	INTRODUCTION TO CURRENT STUDY.....	56
2	METHOD	60
2.1	DESIGN	60
2.2	THE SAMPLES.....	60

2.3	MEASURES	61
2.3.1	The Hospital Anxiety and Depression scale (HADS).....	61
2.3.2	The Chalder Fatigue Scale.....	62
2.3.3	The Family Environment Scale (FES).....	63
2.3.4	The NEO Five Factor Inventory (NEO-FFI).....	64
2.4	PROCEDURE	68
2.5	ANALYSIS	70
3	RESULTS	71
3.1	DEMOGRAPHIC DATA.....	71
3.2	CURRENT PSYCHIATRIC STATUS.....	72
3.2.1	Depression	72
3.2.2	Anxiety	72
3.2.3	Psychiatric Disorder	72
3.3	PRE-MORBID PSYCHIATRIC DISORDER	73
3.3.1	Pre-morbid affective disorder	73
3.3.2	Pre-morbid psychiatric disorder	73
3.4	EMOTIONAL DISTRESS - HADS SCORES.....	73
3.4.1	Exploratory Data Analysis.....	73
3.4.2	HADS Total Score	73
3.4.3	HADS - Depression Scores.....	76
3.4.4	HADS - Anxiety Scores.....	80
3.4.5	HADS 'Caseness' - Anxiety and depression.....	83
3.5	FATIGUE SCORES.....	84
3.5.1	Exploratory data analysis.....	84
3.5.2	Across Main Group Comparisons: CFS and Depression.....	86
3.5.3	Across Sub-group Comparisons : CFS/no depression, CFS/depression and Depression.....	86
3.5.4	The Relationship between Fatigue scores and Emotional distress (HADS -total).....	87
3.5.5	Attributions for Fatigue	88
3.6	PERSONALITY FACTORS.....	91
3.6.1	Exploratory data analysis.....	91
3.6.2	Comparisons across the two main groups: CES and Depression.....	92
3.6.3	Comparisons across Sub-groups: CFS/only, CFS/depression ,depression.....	95
3.6.4	Comparison with Test Norms	99
3.7	DIMENSIONS OF FAMILY FUNCTIONING	101

3.7.1	Exploratory data analysis.....	101
3.7.2	Comparisons across the two main groups: CFS and Depression.....	101
3.7.3	Comparisons across sub-groups: CFS/no depression, CFS/depression and depression.....	102
3.7.4	Comparisons with Test Norms.....	106
4	DISCUSSION	109
4.1	MAIN FINDINGS	109
4.1.1	Psychiatric Comorbidity	109
4.1.2	Psychological distress.....	111
4.1.3	Fatigue.....	112
4.1.4	Personality factors.....	114
4.1.5	Family functioning.....	119
4.2	METHODOLOGICAL LIMITATIONS.....	121
4.3	CONCLUSIONS.....	126
5	REFERENCES.....	128
6	APPENDIX.....	159
Appendix I.	The hospital anxiety and depression scale.....	159
Appendix II.	Fatigue questionnaire	161
Appendix III.	The family environment scale.....	163
Appendix IV.	The NEO five factor inventory	170
Appendix V.	Research information sheet.....	174
Appendix VI.	Instructions for subjects.....	176

1 LITERATURE REVIEW

1.1 INTRODUCTION

Chronic fatigue syndrome (CFS), also commonly known as post viral fatigue syndrome and myalgic encephalitis (ME) is a syndrome characterised by persistent and incapacitating fatigue, which may be accompanied by various other somatic and psychological symptoms, including: aching muscles and joints, headaches, sore throat, painful lymph nodes, muscle weakness, mental fatigue, emotional lability and depression (David, Wessely, & Pelosi, 1988; Holmes, Kaplan, Gautz et al, 1988). The nature and aetiology of chronic fatigue syndrome has been the subject of controversy and debate in recent years and remains poorly understood. Research to date suggests that it is a complex heterogeneous disorder with various sub-types and both biological and psychological features. At the current time, a multi-factorial model of the syndrome appears to be most widely accepted, in which chronic fatigue syndrome or CFS is viewed as a symptom complex which can be reached by various different routes, rather than be determined by a single cause or agent (Wessely, 1996). Much of the controversy surrounding the aetiology of the chronic fatigue syndrome has reflected an 'anti-psychiatry' theme, and a concern on the part of sufferers that the symptoms may be trivialised and dismissed as psychological in origin. Such concerns seem to reflect societal views about what constitutes legitimate suffering. Chronic fatigue syndrome seen as a physical disease implies legitimacy, whereas chronic fatigue syndrome seen as a psychological illness implies personal weakness and malingering (Ware, 1993). The debate can also be seen to reflect the central influence of a 'dualistic' view of illness in Western culture, where

mind and body are viewed as operating separately. Current working models of CFS however, reflect a move away from this dualism and recognise an interactive relationship between psychological and physiological factors.

1.2 HISTORY

CFS has been likened, in its presentation, to the concept of 'Neurasthenia' established by Beard in 1869 (McEvedy and Beard, 1973). This condition was ascribed to social conditions such as exhaustion in the middle classes arising from 'brain work' and other stresses linked with industrialised society. During the same period JM Da Costa (1871) described a clinical syndrome observed in soldiers during and after the American Civil War termed 'Irritable Heart'. This condition was very similar to neurasthenia in terms of its presentation, the important role ascribed to stress in the development of the disorder, and central nervous system involvement in the patho-physiology of the illness. By the end of the century psychological factors were increasingly considered causative in the development of neurasthenia. Paul Wood (1941), an eminent cardiologist, having observed over 300 patients with 'Effort Syndrome', re-evaluated Da Costa's original material and concluded that a complex interplay of psychological and biological risk factors were responsible for the syndrome including; family history, infections, neurosis and physical/mental strain (Demitrack and Abbey, 1996).

In the 1940's and '50's an alternative model emerged to account for these elusive illnesses, arising from research, which examined factors influencing the prolonged recovery from infectious illness. Cluff, Trever, Imboden, & Canter (1959) and Imboden, Canter, & Cluff, (1959; 1961a; 1961b) investigated the role of

psychological factors in delayed recovery from acute brucellosis and flu. It was concluded that in patients with a pre-illness propensity to depression there was a greater tendency for some degree of depressive symptoms to arise during acute infection, the symptoms of which when merged with physical illness could prolong recovery. A comparison report (Kasl, Evans, & Niederman, 1979) to a study by Hallee, Evans, Niederman, Brooks, & Voegtly (1974) at West Point Military Academy in the US found evidence of an association between greater academic pressure and the development of infectious mononucleosis in cadets. Risk factors identified included; having fathers described as 'overachievers', high levels of motivation for success and poorer academic performance. A prospective study at the Medical Research Council Common Cold Unit (Cohen, Tyrrell, & Smith, 1991) concluded that the pattern of results indicated a specific association between psychological stress and resistance to the development of infection.

Another important area of study relevant to current theoretical models of CFS related to epidemic forms of the syndrome, termed "sporadic epidemic neuromyasthenia". From the 1930's to the '50's there were a number of such 'epidemics' reported worldwide, occurring in the midst of local poliomyelitis epidemics. The epidemic at the Royal Free Hospital London (Crowley, Nelson, & Stovin, 1957) has been the subject of continued controversy and discussion and the term 'benign myalgic encephalomyelitis' was used to describe the syndrome (Lancet, May 1956). McEvedy and Beard (1970; 1973) took a particularly dichotomous approach in their study of the original case data and concluded that 'mass-hysteria' accounted for the majority of illnesses seen. This explanation would seem over simplistic and in conflict with current multi-factorial models. More recently, the

theory of chronic fatigue states as sequelae of acute or reactivated Epstein Barr virus infection has become popular as an explanation for the epidemic form of the syndrome and it seems plausible that such outbreaks may be a distinct and specific sub-class of CFS occurring from viral infection.

1.3 DEFINITION OF CFS, IDIOPATHIC CHRONIC FATIGUE AND FIBROMYALGIA

Fatigue is a problematic concept for which precise definition and measurement is difficult due to its subjective and multi-factorial nature.

1.3.1 Chronic fatigue syndrome

Chronic fatigue syndrome was first defined in 1988 (Holmes, et al – Centre For Disease Control, Criteria, US) in terms of primary symptoms of fatigue along with a number of other somatic symptoms (see Table1). To meet diagnostic criteria, fatigue needed to be chronic and associated with a reduction in functional capacity. This definition of CFS excluded people suffering from other physical and psychiatric disorders including major depression. The importance given to the existence of certain somatic symptoms for diagnosis within this definition reflects a belief in a biological aetiology for the disorder involving infection and/or immune dysfunction.

The Oxford criteria (Sharpe, Archard, Banatvala, Borysiewicz et al, 1991), included some features of the original Centre for Disease Control (CDC) criteria but focussed more on the presence of both physical and mental fatigue and with the exception of, substance abuse and psychosis, psychiatric illness did not exclude diagnosis with CFS. According to the Oxford criteria diagnosis required physical

fatigue with a minimum duration of six months, a definite onset and functional impact. These criteria also specified additional criteria for post infectious fatigue syndrome, a sub-type of CFS, which follows or is associated with infectious illness.

The Australian criteria (Lloyd, Wakefield, Boughton, & Dwyer, 1988) again required persistent and disabling fatigue but in addition one of two alternative secondary criteria is required for diagnosis: neuropsychiatric impairment and or abnormal cell-mediated immunity. The definition is therefore the only one to include a laboratory marker in the diagnosis of CFS.

Most recently, Fukuda, Straus, Hickie, Sharpe, Dobbins & Komaroff (1994) revised the original CDC criteria so that people with a psychiatric disorder were not necessarily excluded. Given the recognised overlap between depression and CFS this was considered to be an inappropriate exclusion. Remaining psychiatric exclusions however included; psychotic illness, bipolar depressive disorder, eating disorders and organic brain disorders. Fukuda et al proposed guidelines for the clinical evaluation and study of CFS and other illnesses associated with unexplained chronic fatigue involving the following items; a thorough medical and psychosocial history, a mental status examination, a thorough physical examination and a minimal battery of laboratory screening tests.

Table 1.0 Case Definitions for Chronic fatigue syndrome (Hotopf & Wessely, 1997)

	Min. duration (months)	Functional Impairment	Cognitive/ neuro- psychiatric symptoms	Other symptoms	New onset	Medical exclusions	Psychiatric exclusions
CDC-1988	6	50% decrease in activity	May be present	6 of 8 required	Required	Extensive list of known physical causes	Psychosis, bipolar disorder, substance abuse
CDC-1994	6	Substantial	May be present	4 of 8 required	Required	Clinically important	Melancholic depression, substance abuse, bipolar disorder, psychosis, eating disorders
Australian	6	Substantial	Required	Not specified	Not required	Known physical causes	Psychosis, bipolar disorder, substance abuse, eating disorders
UK	6	Disabling	Mental fatigue required	Not specified	Required	Known physical causes	Psychosis, bipolar disorder, eating disorders, organic brain disease

1.3.2 Idiopathic Chronic Fatigue

Idiopathic chronic fatigue is the classification given for those patients with unexplained fatigue, which persists or relapses for at least six months, but fatigue severity or symptom criteria for CFS are not met (Fukuda et al 1994). Manu, Lane & Matthews (1996) found patients with idiopathic fatigue to be more similar to patients with chronic fatigue syndrome than to patients with a psychiatric diagnosis of major depressive disorder or somatisation disorder and concluded that CFS could be interpreted as a multi-symptomatic and more severe category of idiopathic chronic

fatigue. This view reflects a dimensional approach to classification of CFS rather than a categorical one, where it is assumed that fatigue as a symptom lies at one end of the spectrum with CFS and its associated disorders at the other end.

1.3.3 Fibromyalgia

In addition to certain psychiatric illnesses, CFS shares a number of features with 'fibromyalgia', a debilitating clinical condition characterised by widespread musculoskeletal pain and tender joints. As with CFS, fibromyalgia often develops following a period of acute stress. Research has found extremely high rates of symptom overlap in CFS and fibromyalgia (Buchwald, Sullivan, & Komaroff, 1987; Goldberg, Sumins, Geizer, & Komaroff, 1990) and it has been suggested that these syndrome similarities suggest a common physiological abnormality (Hudson, Goldenberg, Pope, & Schlesinger, 1992; Sternberg, 1993), which may occur along a spectrum of severity.

Clearly the symptoms of each syndrome have much in common and diagnosis of either syndrome would seem to depend upon the dominant presenting symptoms. Most of the evidence seems to suggest that both syndromes are heterogeneous conditions of mixed aetiology, and for treatment purposes treating the syndromes as equivalent would seem justified. However, the current lack of clear understanding in relation to fatigue syndromes is such that for research purposes it would seem important to delineate the conditions using specific diagnostic criteria.

1.4 EPIDEMIOLOGY

Early studies found prevalence estimates of CFS ranging between 2,800 per 100,000 (Calder, Warnock, McCartney & Bell, 1987) and 3 to 5 per 100, 0000 (Behan & Bell, 1985). Chalder (1998) attributes these differences to the absence of a numerically defined study population as well as standardised criteria. Subsequent studies, which have directly surveyed subjects in epidemiological samples, have estimated rates of CFS varying between 0.07 and 1.8% depending on the criteria used (Bates, Schmidt, Buchwald, Ware, Lee, Thoyer, & Komaroff, 1993; Buchwald, Umati, Kith, Pearlman, & Komoroff, 1995; Lawrie & Pelosi, 1995; Wessely, Chalder, Hirsch, Wallace, Wright, 1996). Chalder (1998) suggests that the high rates found in later studies were probably due to greater awareness of CFS, self-labelling and presentation to GPs.

Several studies have found evidence that the demographic and psychiatric associations of CFS are different in community samples compared with hospital populations (Buchwald et al, 1995, David 1991; Euba, Chalder, Deale, & Wessely, 1996; Lawrie and Pelosi, 1995; Hickie Lloyd, Broughton, Spencer, & Wakefield, 1990). It has been suggested that the process of onward referral from GP to hospital specialist is 'filtered' by such factors as symptom severity, psychosocial stresses, socio-economic status and the patient's attitude to illness (Goldberg and Huxley, 1992) and that these factors may be particularly pertinent for patients with CFS (Lawrie, Manders, Geddes, & Pelosi, 1997; Scott, Deary & Pelosi, 1995). These studies highlight the fact that most subjects seen in specialist centres are atypical of CFS patients generally and the role of selection bias in studies carried out on a hospital population.

1.5 AETIOLOGY

Much of the research relating to aetiology has reflected, to some extent, the dualistic view of illness and disease that predominates in Western Culture. A linear cause-effect model, in which, pathological agents lead to bodily symptoms, has been assumed (Singh, Nunn, Martin & Yates, 1981). More recently there has been progress away from this dualism towards more complex multi-factorial models of CFS in which organic and psychological features are seen as interactive (Taerk, Toner, Salit, Garfinkel, & Ozersky, 1987; Wessely, David, Butler & Chalder, 1989,).

1.5.1 Biological Models

A number of biological models have been proposed, the most prominent of which are reviewed briefly here.

The Role of Viruses

Many patients report having experienced a viral infection at the onset of their fatigue (Wessely & Powell, 1989) and regard this as the cause of their symptoms. An infectious aetiology is also suggested by the presence of cluster epidemics, a consistency of reported symptoms and the presence of immune abnormalities. However, despite reports that patients may have chronic viral infections including; Epstein-Barr (EB) Virus, Chronic Enterovirus, and Human Herpes Type 6, ten years of research has not provided convincing evidence to support this theory of chronic infection (Farrar, Locke, & Kantrowitz, 1995). With the exception of EB virus there is no convincing evidence that common viral infections are a risk factor in chronic

fatigue syndrome though delayed recovery occurs in a small percentage of patients following some more serious infections such as glandular fever (White, Thomas, Amess, Grover, Kangro & Clare, 1995b) and meningitis (Hotoph, Noah, & Wessely, 1996). It has been suggested (Wessely, 1996) that viral infections are best viewed as one of several possible aetiological factors in chronic fatigue syndrome.

Chronic Immune Dysfunction

Related to the theory of persistent viral infection the immunological model proposes that a precipitant infection or some other antigenic challenge provokes a disordered immune response that is inappropriate and more persistent than necessary (Gold, Bowden, Sixby et al, 1990; Lloyd, Wakefield, & Hickie, 1993). A number of abnormalities have been shown in the immune system of patients with CFS (Straus, Fritz, Dale, Gould, & Strober, 1993; Strober, 1994). However, these findings have not been consistently replicated and the heterogeneity of the groups studied together with methodological difficulties make it difficult to interpret the published findings (Farrar et al, 1995). Furthermore, immunological changes are known to occur in depressed patients (Herbert & Cohen, 1993) and it is therefore possible that the immunological abnormalities seen in CFS patients are due, at least in part, to depression. An accumulating body of evidence suggests a reciprocal interaction between the CNS and the immune system (Arneson, 1991).

Primary Muscle Disorder

Many patients with CFS complain of weakness and post-exertional fatigue. However, studies of muscle function have demonstrated muscle strength, endurance and fatigability is normal in most patients (Lloyd, Hales, & Gandevia, 1988; Stokes, Cooper, & Edwards, 1988). One study (Wessely & Thomas, 1990) found some evidence of a persistent virus in muscle tissue but this has not been replicated and it has been suggested that it is unlikely that this could account for the degree of disability seen in chronic fatigue syndrome patients (Chalder, 1998). Finally, this theory could not account for the mental fatigue commonly reported in CFS and central mechanisms would seem more likely to underlie the experience of fatigue (Chalder, 1998). Central mechanisms are supported by evidence of dysfunction in the neuroendocrine system and central neurotransmitter dysregulation (Cleare, Bearn & Allain, 1995; Demitrack, Dale, Strauss et al 1991). Such dysregulation would seem to explain more satisfactorily the wide-ranging symptoms of fatigue reported by CFS patients and associated negative emotional states: irritability, depression, pain, frustration and anxiety (Cameron; 1973, Berrios, 1990). Similar high levels of central and peripheral fatigue reported by patients with CFS and patients with depression (Wessely & Powell, 1989), would seem to support the idea of a common mechanism underlying fatigue in both disorders involving biochemical dysregulation.

Neuroendocrine Disorder

Many of the clinical manifestations of CFS, such as fatigue resemble the features of mild glucocorticoid deficiency and it is proposed that patient's with CFS have a

functional abnormality of the hypothalamic pituitary system causing secondary impairment in adrenal function (Demitrack, Dale, Straus et al, 1991). Abnormal corticosteroid levels in CFS patients may disrupt immune functioning and impair the ability to respond to stress. It has been suggested that the neuroendocrine system (Hypothalamic-Pituitary-Adrenal Axis) may play a central role in the mechanisms by which mood and reaction to stress modulate immunity in CFS and this theory is considered in more detail later on when considering the relationship between psychiatric disorders and chronic fatigue syndrome.

Primary Sleep Disorder

Most patients with CFS have sleep disorders, which are likely to cause daytime fatigue (Morris, Sharpe, Sharpley, Cowen, Hawton & Morris, 1993). Sleep laboratory research has demonstrated that patients with CFS have a specific lack of normal deep (non-REM) sleep (Moldofsky, 1993). Sleep disturbances are known to cause daytime sleepiness, impaired attention and concentration, muscle aches, depressed mood and impaired immunological functioning. More specifically a study by Irwin, Smith & Gillin (1992) found that total sleep time, sleep efficiency and duration of non-REM sleep were positively correlated with natural killer cell activity. Taken together, it has been concluded that sleep disturbance may contribute significantly to the patho-physiology of chronic fatigue syndrome (Farrar et al 1995)

1.5.2 Psychiatric/Psychosocial Models

These models are considered in depth in the proceeding section of this literature review, which deals with the overlap between CFS and depression. Very briefly,

psychiatric models of CFS include, firstly the theory that chronic fatigue syndrome is an atypical manifestation of a depressive disorder in which somatisation and central nervous system/autonomic nervous system involvement may explain the prominence of fatigue and somatic symptoms. Secondly, the 'depression-vulnerability hypothesis' suggests that the disorder occurs in individuals with a pre-morbid vulnerability to depression and prolonged dysfunction associated with CFS may be attributable to major depressive disorder (Salit, 1985; Taerk et al, 1987; Wessely et al, 1989). This model, while emphasising the role of depression in CFS, recognises an interplay between organic and psychological factors and may be equally considered to be a multi-factorial/interactive model of CFS. The cognitive behavioural model of chronic fatigue syndrome (Surawy, Hackmann, Hawton & Sharpe, 1995) expands upon the depression-vulnerability hypothesis and emphasises the role of cognitive factors in determining vulnerability to CFS and symptom maintenance. Other theories, which have been proposed to explain the relationship between depression and CFS, are considered later.

A third psychiatric model proposes that CFS arises from a basic vulnerability to stress and operates through a number of different pathways. Psychoneuroimmunology research has shown that immune dysfunction can be suppressed by a variety of stresses and negative life events (Herbert and Cohen 1993; Kiecolt-Glaser & Glaser, 1992). Amongst CFS sufferers negative life events and a hectic pace of life were prominent personal themes (Ware, 1993). According to this theory, stress is seen as central in the causation of chronic fatigue syndrome, integrating the functional interaction of the nervous, endocrine and immune systems. Goldberg and Huxley's 1992 bio-social model of mental illness asserts that there are

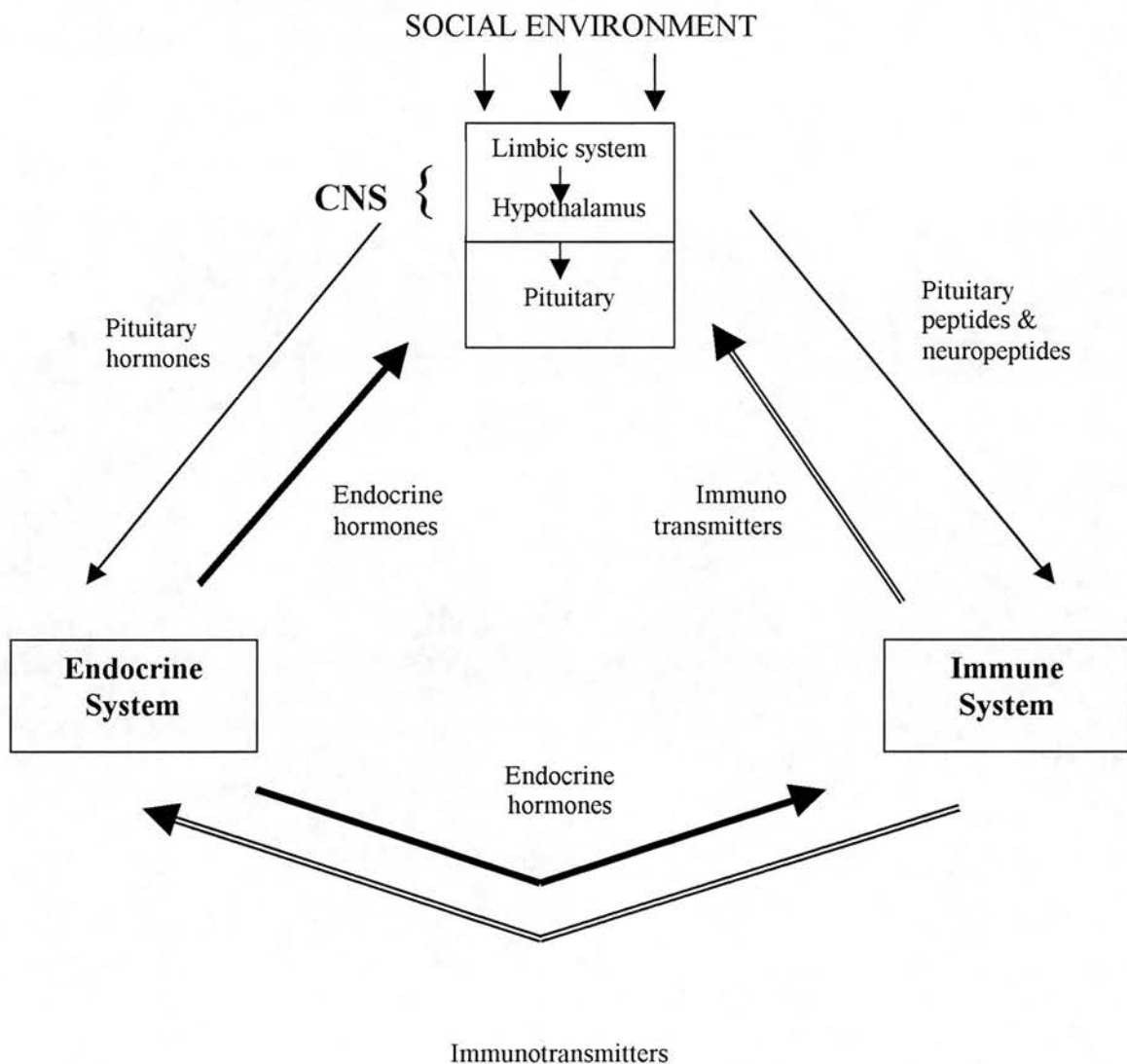
only a very limited number of ways that human beings respond to psychological stress and that these are defined by two underlying dimensions of symptomatology, anxiety and depression, which often occur in combination. They suggest that it may be useful to think of another dimension representing neurasthenic symptoms, but at present this is not justified and such symptoms are seen to represent a chronic mild form of symptom experience, with symptoms, which load on both anxiety and depression. Goldberg and Huxley describe a model relating social environment and stress to psychological and physical health involving three independent but related systems: the CNS, neuroendocrine system, and immune system, which are used to explain reduced immunocompetence and illness in response to stress. The relationship between the three systems and the social environment is depicted in Fig 1.0.

The CNS acts as the major controller, translator and integrator of stimuli arriving from the environment and also controls the adaptive response to the environment. The activation of both sympatho-adrenal and hypothalamo-pituitary axes leads to complex processes that have negative effects on immune function. This model is supported by several studies (Bartrop, Luckhurst, Lazarus, Kiloh, & Penny, 1977; Irwin, Donnelly, Risch, Bloom, & Weiner, 1988), which found relationships between impaired immune responses and depression/bereavement.

Cortisol is the hormone released by the adrenal cortex in response to stress and a relationship has been found between high levels of cortisol and a decrease in the immune response (Fauci and Dale, 1974). Cortisol is also thought to enhance the

activity of 5HT pathways (Cowan and Anderson, 1985) and it is suggested that this may lead to breakdown of resilience and depression.

Fig 1.0 The Relationship between social events and three bodily systems (adapted from Goldberg & Huxley 1992)



1.5.3 Multi- factorial Models and Multiple Aetiologies

Wessely (1996) reviewing the literature concluded that CFS is a heterogeneous condition that is multi-factorial in origin, with some patients' symptoms associated with psychiatric diagnosis, some with viral illness, and some with abnormal exercise responses. According to this model, CFS is not a single diagnostic entity but a symptom complex, which may be reached by different routes, the end stage of a multi-factorial process. Jordan, Landis, Downey, Osterman, Thurm & Jason, 1998) advocated a diathesis-stress model of CFS, in which life-stresses produce the disease state in individuals with a constitutional predisposition. It is suggested that different causative factors may result in slightly different presentations of CFS. Demitrack and Abbey (1996) proposed a 'risk factor model' in which they rejected the notion of a unitary etiological event explaining the symptoms of CFS and emphasised the interaction between disparate factors including; stress, personality and concurrent psychiatric illness which may be linked with immunological changes which themselves may lead to slow recovery from viral and other infections. It is suggested that the relative contribution of each factor in increasing the risk of developing CFS in any individual may be difficult to specify with any certainty. This model combines several aetiological theories and provides an attractive way of conceptualising CFS amidst the current confusion regarding its causes, and a useful assessment tool. However, there does not appear to be any empirical evidence to support the theory of additive risk factors and the model is unable to specify the relative contribution of different factors to risk for any individual. It may therefore be equally justifiable to assume multiple aetiologies for

CFS, with different causes in each case rather than a combination of contributing factors.

1.6 THE OVERLAP BETWEEN PSYCHIATRIC DISORDER AND CHRONIC FATIGUE SYNDROME

Several studies have found evidence of a strong relationship between symptomatic fatigue and psychological distress. A large-scale survey (Pawlikowska, Chalder, Hirsch, Wallace, Wright & Wessely, 1994), found a correlation of 0.6 between scores on the fatigue scale (Chalder et al, 1993) and the General Health Questionnaire (Goldberg, 1972). This correlation was replicated in another study (Lawrie & Pelosi, 1995). Another study (Walker, Katon, & Jemelka, 1993) found individuals who met criteria for symptomatic fatigue had increased rates of depression, dysthymia, and somatisation disorder.

Studies, which have investigated the overlap between CFS and psychiatric disorder, have reported a number of psychiatric diagnoses relating to CFS, the most common of which are mood disorders, anxiety disorders and somatoform disorder (David, 1991; Farrar et al, 1995; Manu Lane & Matthews, 1992). Reviewing the literature, Farrar et al found 50 to 75 per cent of CFS patients fulfilled operational criteria for psychiatric disorder (Kruesi, Dale & Straus 1989; Lane Manu & Matthews, 1991). A large prospective primary care study (Wessely et al, 1996) found subjects with chronic fatigue were at greater risk for current psychiatric disorder, assessed by standardised interview (60 per cent versus 19 per cent non Chronic Fatigue). Both the prevalence and incidence of CFS were associated with measures of previous psychiatric diagnoses. Another study (Euba et al, 1995)

compared patients with CFS drawn from a community sample with those seen in tertiary care. Rates of psychological distress were similar in both groups, suggesting that the high rates of depression seen in CFS were not due to a selection bias.

1.6.1 Mood Disorders

The occurrence of mood disorders in chronic fatigue syndrome in patients has received the most study of all the psychiatric diagnoses and would seem to co-occur with CFS most commonly (Manu, Lane & Matthews, 1988; Ray, 1991; Salit, 1985; Taerk et al, 1987). Manu et al (1992) cited five research groups demonstrating the high frequency depression amongst patients with chronic fatigue syndrome, the lifetime prevalence ranging from 46 to 75 per cent (Hickie, Lloyd, Wakefield, & Parker, 1990; Kruesi et al, 1989; Lane et al, 1991; Taerk et al, 1987; Wessely & Powell, 1989). Three of these studies found major depressive disorder predated the onset of Chronic Fatigue (Kruesi et al, 1989; Lane et al, 1991; Taerk et al, 1987) while one study (Hickie et al, 1990) found the prevalence of premorbid major depression (12.5%) and total psychiatric disorder (24.4%) in patients with CFS was no higher than those estimated for the general community. Major depression was diagnosed in 22/46 CFS patients, but only 6 cases could be diagnosed as to have a mood disorder before the onset of CFS.

Other studies have compared psychiatric illness in chronic fatigue syndrome patients and patients with other neuro-muscular and central nervous system diseases. Katon, Buchwald, Simon, Russo, & Mease (1991) compared patients with CFS (N=79) to patients with rheumatoid arthritis (N=31). Patients with chronic fatigue

had a higher prevalence of major depression and somatisation disorder than patients with rheumatoid arthritis and a significantly higher prevalence of current and lifetime diagnoses. Similarly, Wessely and Powell (1989) compared patients with unexplained chronic fatigue syndrome (N=47) with a group of patients with fatigueing neuro-muscular diseases and in patients with major depressive disorder. It was found that 72 per cent of post-viral fatigue syndrome patients were cases of psychiatric diagnoses using criteria, which excluded fatigue as a symptom, compared with 36 per cent of the neuro-muscular group. Attribution of symptoms to physical rather than psychological causes was the principal difference between chronic fatigue syndrome patients and psychiatric controls. Interestingly, it was found that CFS patients had high levels of central and peripheral fatigue, whereas those with neuromuscular disorders suffered from peripheral fatigue and only complained of central fatigue if they were also depressed. When compared with patients with depression, those with CFS had similar levels of central and peripheral fatigue. It has been suggested that the experience of each type of fatigue may involve different mechanisms and that individuals with CFS may have the same mechanism as those with depression (Hoptopf & Wessely, 1997). Similarly a study by Wood, Bentall, Gopfert & Edwards (1991) comparing patients with CFS (N=34) and a neuro-muscular group (N=24) found significantly fewer of the muscle group were diagnosed as having a psychiatric disorder, with the relevant risk of psychiatric diagnosis in the two groups of 3.3: 1.

A study by Pepper, Krupp, Friedberg, Doscher, & Coyle (1993) compared a group of patients with CFS to a group of patients with multiple sclerosis and major depressive disorder. Higher levels of depression symptoms and more frequent

diagnoses of current depression were found in the CFS group compared with the multiple sclerosis group. However, the CFS group were found to be significantly less depressed with fewer personality disorders than the major depressive disorder group. In addition, the lifetime prevalence of psychiatric diagnosis in CFS patients (51%) was lower than that previously found by other investigators (Kruesi et al, 1989; Lane et al, 1991; Taerk et al, 1987) but higher than that found by Hickie et al (1990). The authors suggest that this may have been due to the use of a more accurate diagnostic measure in their study and subject selection. The patients in their study were seen by a neurologist rather than a mental health professional thereby introducing selection bias possibly affecting the frequency of reported psychiatric symptoms in their sample.

The studies relating to mood disorders in patients with CFS can be criticised on a number of grounds. Firstly, these studies were conducted in a variety of hospital settings and are therefore subject to selection biases. Patients recruited from specialist populations are probably not representative of CFS patients in the general population and subject characteristics are likely to differ depending upon the emphasis of the specialist setting in which they are seen, for example, neurological or psychiatric. Secondly, diagnostic criteria for CFS varied between studies as did diagnostic measures for depression. Despite these criticisms, the high frequency of depression and higher lifetime prevalence of major depression in patients with CFS would seem in little doubt. However, the shortcomings of these studies make it difficult to draw conclusions about aetiology. The evidence regarding the time of onset of depressive illness is contradictory, although three out of four studies, which have examined this issue, would seem to lend support for the hypothesis of

depression as a vulnerability factor in the development of CFS. Further research drawing CFS patients from a primary care population and addressing the above criticisms would seem necessary to clarify the relationship between CFS and depression.

1.6.2 Somatisation Disorders

The relationship between Chronic fatigue syndrome and somatisation disorders specifically and somatisation and medically unexplained symptoms more generally has spurred considerable discussion (Abbey, 1996). Somatoform disorders have received relatively little study in chronic fatigue syndrome samples apart from the diagnosis of somatisation disorder. Reviewing the literature Abbey (1996) cites studies in which somatisation disorder has been assessed in samples of patients with chronic fatigue (Manu et al, 1989a) and chronic fatigue syndrome (Hickie et al, 1990; Katon et al, 1991; Kruesi et al, 1989; Wessely et al, 1989; Wood et al, 1991). These studies have found increased rates of somatisation disorder in patients with CFS. In the study by Manu et al (1989a) one hundred patients attending a chronic fatigue clinic were assessed, fifteen of which were diagnosed using the diagnostic interview schedule to have somatisation disorder. This group had a mean age of onset of 16.3 years and 23.5 years for fatigue. In a larger cohort from the same group, somatisation disorder was diagnosed using the diagnostic interview schedule in 28 per cent of 60 patients meeting CDC criteria for chronic fatigue syndrome and in only five per cent of fatigued age and gender-matched controls from the same cohort. When abridged criteria for somatisation was used (Escobar, Burnam, Karno, Forsythe, & Golding, 1987; Escobar, Manu, Matthews, Lane, Swartz, & Canino,

1989) a much higher percentage of individuals were identified demonstrating significant somatisation – 73 per cent of the CFS subjects and 51 per cent of controls when all the symptoms were used, 67 per cent and 43 per cent prospectively when abridged criteria did not include symptoms characteristic of CFS. Interestingly 88 per cent of the chronic fatigue syndrome patients meeting criteria for somatisation disorder had experienced significant functional somatic symptoms prior to the onset of CFS with the first symptom generally occurring in childhood. Functional somatic symptoms have been defined as physical symptoms, which do not appear to have an organic explanation and are thought to originate predominantly from psychological and social factors (Sharpe, Mayou, & Bass, 1995). Johnson, DeLuca & Natelson (1996) concluded that the diagnosis of somatisation in chronic fatigue syndrome is ambiguous with rates varying from 5 to 15 per cent (Clark & Katon, 1994, Lane et al, 1991). However, they emphasised that this would not preclude the chronic fatigue syndrome patients from somatising in the broader sense, a behaviour that may be influenced by neuroticism. This theory would seem to be supported by results of a study by Wessely & Powell (1989) which concluded that somatisation was more prominent in chronic fatigue syndrome patients compared with patients with major depression and neuro-muscular disease and constituted the principal difference between chronic fatigue syndrome and affective disorders. This broader concept of somatisation, particularly in relation to depression and anxiety disorders, is discussed later. Similarly Abbey and Garfinkel (1991) conclude that preliminary psychometric evidence of the degree of somatisation in CFS is contradictory. Singer, Thompson, Kraiuhin, Gordon, Howe, Howson & Meares, (1987), found a degree of somatic preoccupation, hypochondriasis and affective inhibition in a small sample of patients with post-viral fatigue syndrome was comparable to that found in patients with

somatisation disorder. However Hickie et al (1990) using the same measure found no excessive hypochondriasis or affective inhibition with patients with CFS and believed that their attribution of symptoms to physical illness was understandable.

1.6.3 Personality

In the late fifties and early sixties, research (Cluff et al, 1959; Imboden et al, 1959, 1961a; 1961b) concluded that for patients with a pre-illness propensity to depression there was a greater tendency for prolonged recovery from acute brucellosis and flu. More recent studies, which have examined personality pathology in chronic fatigue syndrome patients, have produced contradictory findings. Millon, Salvato, Blaney, Morgan, Mantero-Atienza, Klimas, & Fletcher (1989) found patients with CFS scored above the level considered indicative of pathology on the following personality scales: histrionic (33 per cent of subjects), schizoid (29 per cent), avoidant (25 per cent), narcissistic (25 per cent) and aggressive/sadistic (25 percent). The relative frequency of higher scores for three of these scales: histrionic, schizoid and avoidant were greater than for controls without significant psychiatric disorder. Similarly, a study by Blakely, Howard, Sosich, Murdoch, Menkes & Spears (1991) compared the psychological characteristics of chronic fatigue patients (N=58) with a comparison group of chronic pain patients (N=104). Considerable overlap was found between the two groups in terms of the Minnesota Multiphasic Personality Inventory (MMPI) 'neurotic triad', but chronic fatigue syndrome patients showed more deviant personality traits reflecting raised levels of 'emotionality' (MMPI factor). Stricklin, Sewell, & Austrad (1988) comparing 25 women with epidemic neuromyasthenia (the epidemic form of post viral fatigue syndrome) with 25 healthy

women using the MMPI found similar elevations. Blakely et al (1991) concluded that their results were consistent with the hypothesis of 'emotionality' as a predisposing factor in chronic fatigue syndrome, possibly increasing vulnerability to other causative factors. The results were considered to be consistent with the suggestion of pre-morbid personality traits predisposing to chronic fatigue syndrome (Imboden et al, 1961a; 1961b; Komaroff, 1988). Evidence from psychoneuroimmunology research was also cited by Blakely et al (1991) demonstrating that psychological status is correlated with reduced immunocompetence and enhanced vulnerability to illness (Rosenhan & Seligman, 1988). One study by Hiesel, Locke, Kraus, & Williams (1986) demonstrated a negative correlation for all scales of the MMPI, except two, and natural killer T-cell function. The MMPI comprises 13 basic clinical scales, which load on either of two factors: neuroticism and introversion. Similarly, other psychoneuroimmunology research has demonstrated a relationship between reduced immunocompetence and depression/bereavement (Bartrop et al, 1977; Irwin et al, 1988). These research findings appear to be consistent with the Goldberg and Huxley model of physical and mental health described previously. Furthermore the findings in relation to personality and CFS would seem explainable both in terms of the stress model of CFS and the depression-vulnerability hypothesis. It may be hypothesised that increased neuroticism and consequent vulnerability to stress leads to the development of anxiety and/or depression and reduced immunocompetence, through the mechanisms described by the Goldberg and Huxley model. Alternatively, in the same way, individuals with increased emotionality may be more likely to develop depression as a consequence of infection, which may then perpetuate physical symptoms through reduced immunocompetence.

Other studies, which have examined personality factors in fatigue more generally, have also found similar associations. In study by Kroenke, Wood, Mangelsdorff, Meier & Powell (1988) primary care patients complaining of fatigue were found to be more sensitive and inhibited and less sociable than those who were not tired. Montgomery (1983) found that 'uncommonly tired' college students were reported to be more introverted, less emotionally stable and more competitive than those who were not tired. Wood, Magnello & Jewell (1990) found a positive association between neuroticism and fatigue and a negative association between extroversion and fatigue. Reviewing the literature, Manu et al (1992) concluded that the majority of patients with CFS have abnormal personality traits. Johnson et al (1996) concluded that overall these studies suggest a tendency for histrionic and emotional type traits to be over represented in chronic fatigue subjects. However, it is suggested that studies of personality in chronic fatigue populations suffer from methodical flaws ranging from a lack of a control group (Millon et al, 1989), using the MMPI without correcting physical symptoms (Blakely et al, 1991), and not using CDC criteria for chronic fatigue syndrome (except Millon et al's 1989 study). Johnson et al's study (1996) produced contradictory findings regarding personality pathology in chronic fatigue syndrome. This study compared individuals with CFS (N=35) with healthy controls (N= 35) and two other fatiguing illness groups – mild Multiple Sclerosis (N=20) and depression (N=24). CFS subjects were found to display higher frequencies of a variety of DSM III-R Axis II personality disorders and elevated levels of neuroticism compared with controls. However personality pathology in the CFS group did not differ from that exhibited by subjects suffering from MS. Both groups were significantly less compromised relative to patients with major depression. Similarly, a study by Pepper, Krupp, Friedberg, Doscher, & Coyle

(1993) comparing three groups of patients; CFS, MS and MDD found that the CFS group had significantly less depression and fewer personality disorders than the depressed group. A more recent study (Christodoulou, DeLuca, Johnson, Lange, Gaudino, & Natelson, 1998) compared the personality profiles of 38 CFS subjects with 40 healthy controls and 40 subjects with MS. Subjects were examined within Cloninger's biosocial theory of personality. Both illness groups displayed similarly elevated levels of harm avoidance and lower levels of reward dependence than healthy controls, in accord with Johnson et al's (1996) finding of elevated neuroticism, a related trait. The hypothesis that CFS is any more likely than MS to be the result of a premorbid negative view of life was therefore not supported by these findings. However, it is possible that the two groups came to display similar profiles for different reasons, CFS solely because of predisposing personality traits and MS solely in response to chronic illness. This study also found that the CFS subjects displayed preserved "persistence" whereas the MS group showed a reduction compared with healthy controls. . It has been proposed that "persistence" could conceivably exacerbate the level of fatigue experienced by a chronically ill person and therefore be maladaptive in persons with CFS. This finding is in keeping with reported high levels of "action-proneness" in CFS patients as compared with neurotic patients and those with chronic organic conditions (Houdenove, Onghena, Neerinckx, & Hellin, 1995) and with those pre-morbid personality features reported by Surawy et al (1995) which included; marked achievement orientation, perfectionism, high standards for work, performance, responsibility and personal conduct. The cognitive-behavioural model of CFS offers an explanation for the way achievement-orientation as a feature of premorbid personality contributes to the maintenance of fatigue and depression in CFS. Perfectionism has been implied as a

vulnerability factor in the development of unexplained fatigue, more generally. In a study by Magnusson, Nias, & White (1996) different components of fatigue and perfectionism were studied in 121 female nurses. The results indicated that neuroticism as well as negative perfectionism was separately associated with trait fatigue. Perfectionism has been found to be associated with both depression and anxiety (Flett, Hewitt, Blankstein & O'Brien, 1991) and used as a maladaptive coping strategy by people scoring high on neuroticism. Most recently a large study by Wood and Wessely (1999) challenged the view of premorbid personality proposed by the cognitive behavioural model of CFS. In this study 101 CFS patients were compared with 45 rheumatoid arthritis (RA) patients on a range of standard questionnaire measures. No differences were found between CFS and RA patients on measures of perfectionism, attitudes towards mental illness, defensiveness, social desirability or sensitivity to punishment (a concept related to neuroticism). However social adjustment, based on subjective assessment of overall restriction of activities and relationship difficulties was substantially poorer in the CFS group. This was highly associated with depressive symptoms but remained significant even after adjusting for depressive symptomatology. The authors concluded that the stereotype of CFS sufferers as perfectionists with negative attitudes toward psychiatry was not supported

Overall, the research evidence in respect to personality factors in CFS appears limited and conflicting. A number of studies have found evidence of relatively high levels of neuroticism in CFS patients, although it seems probable, that this is only the case for the subgroup of CFS with associated psychiatric morbidity. There is little systematic evidence to support those pre-morbid personality features

proposed by the cognitive behavioural model of CFS: perfectionism and achievement orientation.

1.7 THE RELATIONSHIP BETWEEN DEPRESSION AND CHRONIC FATIGUE SYNDROME

The view of CFS as primarily a depressive disorder is supported by the relatively large number of studies, which have demonstrated evidence of psychiatric disorder, predominantly depression, in CFS patients (Kruesi et al, 1989; Lane et al, 1991; Manu et al, 1988, 1989b; Salit, 1985; Taerk et al, 1987). However, conceptual and methodological ambiguities make it difficult to interpret the evidence (Ray, 1991) and a causal relationship between depression and CFS cannot be assumed from their association. Thirty to fifty per cent of CFS sufferers show no evidence of clinically significant depression and emotional problems have been found to be less common in the context of primary care (Wessely, 1989). It also provides no explanation for the identification of other co-existing disorders including anxiety disorder, somatisation disorder and undifferentiated psychiatric morbidity. There is also the major issue of diagnostic ambiguity and the nature of depression in CFS. With regard to the latter, it has been questioned whether CFS patients show the same low self esteem and self critical thinking which is a central feature of major depressive disorder (Powell, Dolan, & Wessely, 1990). It has been suggested (David et al, 1988b) that a finer description of the phenomenology of depression is needed in charting the overlap and divergence between CFS and depression.

Various hypotheses have been proposed to account for the relationship between CFS and major depressive disorder (Abbey and Garfinkel, 1991; Ray,

1991). Each of these hypotheses is considered in turn.

1.7.1 CFS as an atypical manifestation of major depressive disorder

This hypothesis considers CFS to be an atypical mood disturbance with somatic overlay (Wessely & Powell, 1989), or a somatisation disorder where dysphoria is expressed in bodily terms (Wessely, 1990). The fact that depressed patients in psychiatric settings produce large lists of physical symptoms and the success of anti-depressant medication in treating the symptoms of CFS (including non-mood related) has been suggested as evidence for this model. A number of studies have demonstrated the overlap between depression and somatic symptoms (Kroenke et al, 1988; Manu et al, 1988; Wilson, Widmer, Cadoret, & Jüdesch, 1983). Abbey and Garfinkel (1991) assert that the clinical presentation of depression is very diverse and varies with clinical setting, somatic symptoms being most common in primary care. Lipowski (1990) cited several reports (Bridges & Goldberg, 1985; Prestidge & Lake, 1987) indicating that eighty per cent of patients suffering from depression, evaluated by primary care physicians, presented with physical and not psychological complaints. Another study (Hamilton, 1989) involving 499 people with major depressive disorder found symptoms of both anxiety and fatigability in eighty per cent of the sample. Similarly Wessely & Powell (1989) found no significant difference between a group of CFS patients and depressed patients on measures of either physical or mental fatigue.

Some authors, for example, Fisch (1987) have promoted the term 'masked depression', defined as a depressive illness in which affective and cognitive features

of depression are masked by symptoms such as pain, hypochondria or both. Chronic fatigue syndrome has similarly been viewed as a form of depression with primarily somatic expression. Abbey and Garfinkel (1991) suggest two main processes which may underlie the somatic symptoms of depression, firstly, somatisation and secondly, alteration in the function of the central nervous system and autonomic nervous system.

Somatisation

Somatisation and its relationship with depression, personality and development are given detailed attention in this literature review as these aspects relate directly to the hypotheses tested in the current research. Somatisation has been defined as:

“ The tendency to communicate emotional distress in the form of physical symptoms and to seek help for them.” (Lipowski, 1988, page 1359)

Somatisation is a ubiquitous phenomenon which may occur transiently in healthy individuals in distress, may become a chronic state, or may occur in conjunction with other psychological disorder particularly anxiety and depression (Lipowski, 1986)

There exists a number of distinct, though overlapping theoretical explanations for functional somatic symptoms. One popular theory put forward to explain the process of somatisation is the psychodynamic idea that it serves a defensive function and preserves self-esteem, physical symptoms being more ‘acceptable’ to the individual concerned than ‘psychological distress’ (Katon, Kleinman, & Rosen, 1982). The term ‘alexithymia’ describes the inability to label or to communicate emotional distress and it has been proposed that individuals who somatise score highly on this scale. However it has been found that contrary to what would be

predicted by this theory, somatisation is not associated with an inability to report emotional distress (Simon & Von Korff, 1991). It has been suggested that somatising patients and psychosomatic patients with alexithymia fall at opposite ends of the spectrum of symptom severity (Simon & Von Korff, 1991). Alexithymic patients may have as much difficulty expressing somatic distress as emotional distress, while somatising patients may suffer from heightened sensitivity to both physical and emotional distress. This theory is supported by a recent study (Honkalampi, Hintikka, Tanskanen et al, 2000), which found alexithymia to have a close relationship with depression in the general population. Several other investigators (Pennebaker, 1982; Petrie, 1978) have described individuals who characteristically amplify symptoms, especially at times of emotional distress. Barsky (1988) coined the term 'somatosensory amplification' to describe these tendencies. Instead of viewing physical symptoms as a defence against awareness of affect, this model views physical and psychological symptoms as parallel and equally valued expressions of distress and is supported by the correlation between psychological and somatic distress. This model is supported by Wessely et al's (1996) study, which found that the number of symptoms characteristic of CFS was closely related to the total number of somatic symptoms and to measures of psychological distress. They concluded that the symptoms thought to represent a specific process in chronic fatigue syndrome might be related to the joint experience of somatic and psychological distress. Wessely & Powell (1989) concluded from a study comparing CFS patients with patients with major depression and neuromuscular disorders that somatisation was more prominent in chronic fatigue syndrome patients and constituted the principal difference between CFS and affective disorders. Although CFS patients tend to attribute their symptoms to

physical rather than psychological causes (Powell, Dolan & Wessely, 1990; Wessely & Powell, 1989), other researchers suggest that CFS patients often do communicate emotional distress as part of their condition and have likened them to 'facultative somatisers' rather than true somatisers (Bridges & Goldberg, 1985). The former term describes those patients who do not attribute their symptoms to physical disease when interviewed by a research psychiatrist although they initially present seeking help for physical problems. In a recent study (Wood & Wessely, 1999) the Toronto Alexithymia scale which measures characteristics that predispose people to develop hypochondriasis and somatisation disorders, was given to 101 CFS patients and 45 rheumatoid arthritis (RA) patients. Scores were found to be greater in the RA group. There would therefore appear to be no reliable evidence to support alexithymia as an explanation for possible somatisation of psychological symptoms in patients with CFS.

Research investigating the relationship between personality and symptom reporting (Andrews, 1990; Pennebaker, 1982) and the relationship between neuroticism and anxiety and depressive diagnoses (Andrews, Stewart, & Harris-Yates, 1990; Tyrer, 1985) has been interpreted as supporting a hypothetical triangular relationship between neuroticism, psychiatric illness and unexplained physical illness (Russo, Katon, Sullivan, Clark & Buchwald, 1994). Gray (1981) hypothesised that neurotic individuals are most sensitive to signals of punishment and are therefore more likely to develop negative affect in aversive situations and the resulting affective states may then lead to increased reporting of physical symptoms. Cloninger (1986) labels this trait as 'harm avoidance' in his tridimensional personality questionnaire. It is proposed that harm avoidance and other traits similar

to neuroticism present risk factors for the development of anxiety, affective disorders and medically unexplained symptoms. Studies relating to personality factors in chronic fatigue syndrome have been reviewed earlier and the findings with respect to neuroticism have been somewhat contradictory. While some studies have found increased neuroticism in common with other somatising conditions (Blakely et al, 1991; Kroenke et al; 1988 Wood et al, 1991). Johnson et al (1996) found a group of chronic fatigue syndrome patients more closely resembled a group of patients with MS than a depressed group, in terms of neuroticism and personality disorder. The 34 per cent of the CFS group with current depression accounted for most of the personality pathology in the CFS group, which would seem to support the view that personality factors link depression and somatic symptoms in some individuals with chronic fatigue syndrome.

In addition to personality factors, a number of other features have been proposed as determinants of somatisation including; age, sex, genetics and past personal and family experience. It is suggested that these factors probably play a role in determining which depressed patients somatise (Lipowski, 1990).

Developmental and family factors

Developmental factors are commonly cited as determinants of somatisation (Bass & Murphy, 1995, Kellner, 1986, Lipowski, 1988). Lipowski has suggested that childhood learning experiences, notably exposure to much physical illness behaviour in the family and being rewarded for physical complaints may predispose a person to use somatisation as a way to communicate emotional distress or cope in interpersonal relationships. Looking at somatisation syndromes cross-sectionally in childhood,

Garraalda (1992) concluded that a characteristic pattern of child personality features, academic concerns, family health problems and styles of family interaction could be discerned. Similarly it was suggested that children with fatigue syndromes and their families share many of the personality and family characteristics of children with somatisation disorder. Specific associations have been described with; perfectionist attitudes/high achievement in the child, and family features including; high achievement orientation, inadequate communication on emotional issues, close involvement and concerns about health issues. Minuchin, Baker, Rosman, Liebman, Millman & Todd (1975) used the terms 'enmeshment', 'overprotectiveness', and 'lack of conflict resolution' to describe these characteristics and ascribed them a prominent role in the aetiology of functional somatic symptoms in childhood. Most of the literature relating to developmental and family factors relates to CFS in childhood and adolescence. No study, to date, has examined family factors in adults with CFS and it remains to be seen whether or not similar family characteristics are associated with CFS in adults. A report to the joint committee of the Royal College of Physicians, Psychiatrists and General Practitioners (Wessely, 1996), having reviewed the literature, concluded that relevant psychological factors contributing to CFS in children may involve a complex family dynamic of involvement, high expectations, limited communication on emotional issues and previous experience of illness. Family functioning and developmental factors can be seen to relate to those psychiatric theories of CFS, which involve somatisation of psychological distress. Also, it can be hypothesised that the high achievement orientation reported for families of children and adolescents with CFS may contribute to the development of perfectionist beliefs considered to be a predisposing factor for the development of CFS in the cognitive-behavioural model of the disorder.

Alterations in central nervous system/autonomic nervous system functioning

The second process proposed to underlie the somatic symptoms of depression involves alteration of the central nervous system and autonomic nervous system. In relation to this mechanism the question arises as to whether CFS as an atypical expression of major depression could account for the immunological abnormalities reported in chronic fatigue syndrome. A number of studies have related stressful life events to the onset of various physiological diseases, sometimes involving mood disturbance as an intervening variable (Murphy & Brown, 1980; Craig & Brown, 1984). Studies investigating the immune function associated with major depressive disorder have found changes in a number of neuroendocrine parameters and in neuro-transmitters that are known to modulate the immune system (Stein, Kellner & Schleifer, 1985; Calabrese, King, & Gold, 1987). In Calabrese et al's study depressed people were found to show blunted T-cell responses to mitogen stimulation invitro, as had been previously found for bereaved people. Similarly natural killer cell activity has been found to be decreased in individuals with depression, the recently bereaved and those experiencing high levels of stressful life events. In summary, Stein et al (1985) concluded that immunity appears to be a component of the complex psychobiology of affective disorder. It has been speculated that the neuroendocrine system (HPA axis) plays a central role in the mechanism by which mood and reaction to stress may modulate immunity. However, David (1991) suggests that the HPA axis may be affected by confounding factors such as sleep disturbance and dietary features of both CFS and depression and should therefore be controlled in the interests of scientific evaluation. More recently differences have been found between CFS patients and depressed patients with

respect to 5-HT neurotransmission (Bakheit, Behan, Dinan, Gray, & O'Keane, 1992; Cleare, Bearn, Allain, et al, 1995; Sharpe, Clements, Hawkins, et al, 1996,) and the stress hormone cortisol (Demitrack, 1997; Cleare et al 1995). Rather than depression resulting in reduced immuno-competence such differences suggest that immune changes in CFS may result from the effects of stress upon these systems rather than being secondary to depression.

1.7.2 The Depression Vulnerability Hypothesis

This model proposes that the prolonged disability associated with CFS may be attributable to major depressive disorder (Salit, 1985; Taerk et al, 1987; Wessely et al, 1989). Within this model CFS is considered to reflect the interplay between organic and psychological factors in psychologically vulnerable individuals with a depressive diathesis. In response to viral infection the individual becomes depressed either as a result of a disturbance in neural functioning or as a reaction to associated disability. The resulting major depressive episode is a source of chronic disability that is labelled CFS.

Support for this explanation comes from the large number of studies, which have found an increased lifetime prevalence of psychiatric disorders in patients with CFS. Wessely et al (1989) emphasise the important role that de-conditioning and inactivity play in perpetuating disability. Reviewing the literature, Farrar et al (1995) suggest that between 25 and 50 per cent of patients with CFS have had psychiatric problems such as depression before the onset of their illness (Katon et al, 1991; Kruesi et al, 1989; Lane et al, 1991; Taerk et al, 1987; Wood et al, 1992). Taerk et al

found a lifetime prevalence of mood disorder in 71 per cent of the patients with post-infectious neuromyasthenia. Fifty per cent of the sample reported at least one episode of affective disorder predating illness. Only 17 per cent of twenty-four matched non-clinical volunteers reported a depressive episode in the twelve months prior to interview with 12 per cent reporting at least one episode over a year ago. Kruesi et al (1989) found chronic fatigue syndrome predated psychiatric illness in only 2 out of 21 cases. Lane et al (1991) identified mood disorders during the lifetime of 45 out of 60 patients with chronic fatigue syndrome (75 per cent). Twenty-six patients (43 per cent) had recurrent episodes of major depression whose onset predated the onset of chronic fatigue by at least one year. There are, however, some methodological difficulties with these studies. In Taerk's study no distinction was made between pre-morbid and total lifetime disorder (which may or may not have occurred inside the current period of illness). When only pre-illness psychiatric episodes are considered, there is only a trend towards increased disorder in comparison to the total lifetime prevalence of the group of healthy controls. Also in Kruesi's study, pre-morbid diagnosis was largely accounted for by anxiety disorders, unlikely to be of major psycho-pathological significance in the development of the syndrome. A study by Hickie et al (1990) also produced slightly different findings. Of 48 patients with CFS, a major depressive episode was diagnosed in 22, during the course of their illness, but only six of these could be diagnosed to have mood disorder before the onset of CFS. The pre-morbid prevalence of major depressive disorder and psychiatric disorder was found to be no higher than community estimates.

Further evidence for depression as a vulnerability factor is provided by cohort studies, which have followed patients after viral illnesses. These studies have

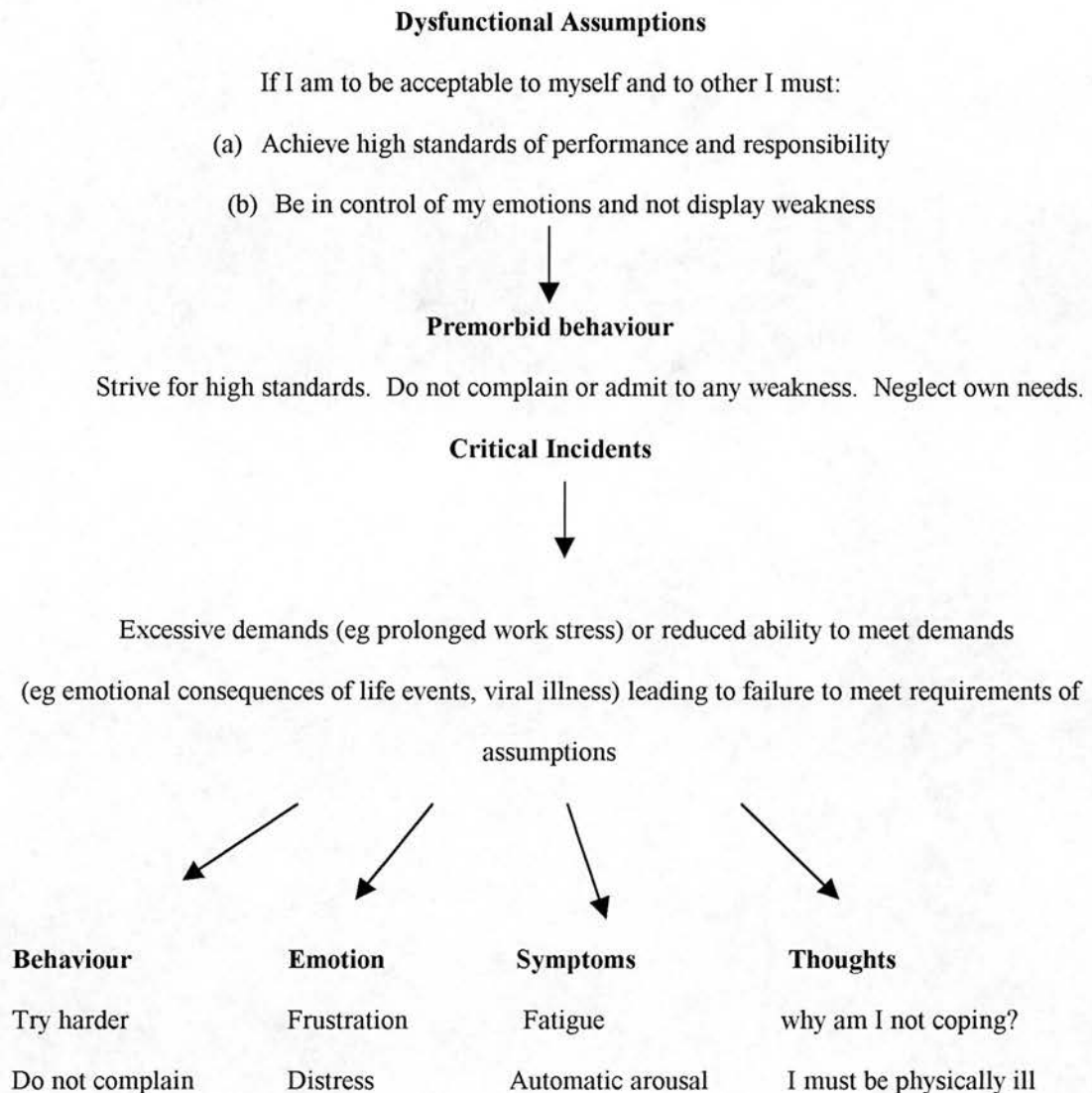
demonstrated that previous emotional disorder or high scores on the GHQ (Goldberg, 1972) are significant predictors of CFS at follow up (Hotopf, Noah & Wessely, 1996; Wessely et al, 1996)

Some of the research investigating personality factors in chronic fatigue syndrome, discussed previously, appears to lend some support for the depression-vulnerability hypothesis (Blakely et al, 1991; Imboden et al, 1959, 1961; Stricklin et al, 1988). These studies have found some evidence of overrepresentation of histrionic and emotional type traits in chronic fatigue syndrome patients (Johnson et al. 1996). It has been suggested that such results are consistent with the suggestion of pre-morbid personality traits predisposing to chronic fatigue syndrome. However these studies suffer from a range of methodological flaws and comparable levels of neuroticism, the personality trait which is linked most closely with vulnerability to psychiatric illness have not consistently been found in CFS and depressed patients (Johnson et al, 1996; Pepper et al, 1993).

Several of the psychiatric and multi-factorial models of chronic fatigue syndrome, described previously, consider that depression is one factor which interacts with other factors resulting in chronic fatigue syndrome and incorporates the idea that pre-morbid vulnerability to depression plays a significant part in the development and maintenance of CFS (Surawy et al, 1995; Wessely et al, 1989). Wessely et al (1989) asserts that the symptoms of chronic fatigue syndrome are caused, at least in part, by depression and physiological decline. Developing these ideas further Surawy et al (1995) proposed that a greater consideration of cognitive factors would provide a more complete explanation of the clinical features of chronic

fatigue syndrome and put forward a cognitive theory of the aetiology of the condition. Within this model predisposing, precipitating and perpetuating factors are considered separately. In relation to predisposing factors, it is proposed that there is a typical pre-morbid personality characterised by: marked achievement orientation, perfectionism, and high standards for work, performance, responsibility and personal control. It is reported that patients also describe themselves 'bottling things up' and 'putting on a brave face'. Precipitating factors are seen as usually involving a combination of psychosocial stress and acute illness. In terms of cognitive theory, the person's perception of his or her inability to perform can be regarded as the 'critical incident', which activates underlying assumptions relating to achievement, strength and personal worth. It is suggested that a typical reaction for such a person is to try even harder to meet targets despite increasing exhaustion and when they are no longer able to do this, the person enters a stage of chronic exhaustion and demoralisation. It is proposed that inability to cope is explained in terms of physical illness, because a psychological condition such as depression would imply weakness or failure, leading to a focus on somatic rather than psychological factors. The cognitive behavioural model appears to incorporate the notion of 'somatisation' as a partial explanation for CFS in terms of the illness beliefs commonly held by individuals with chronic fatigue syndrome. This conceptualisation of the development of CFS is summarised in Fig. 2.0.

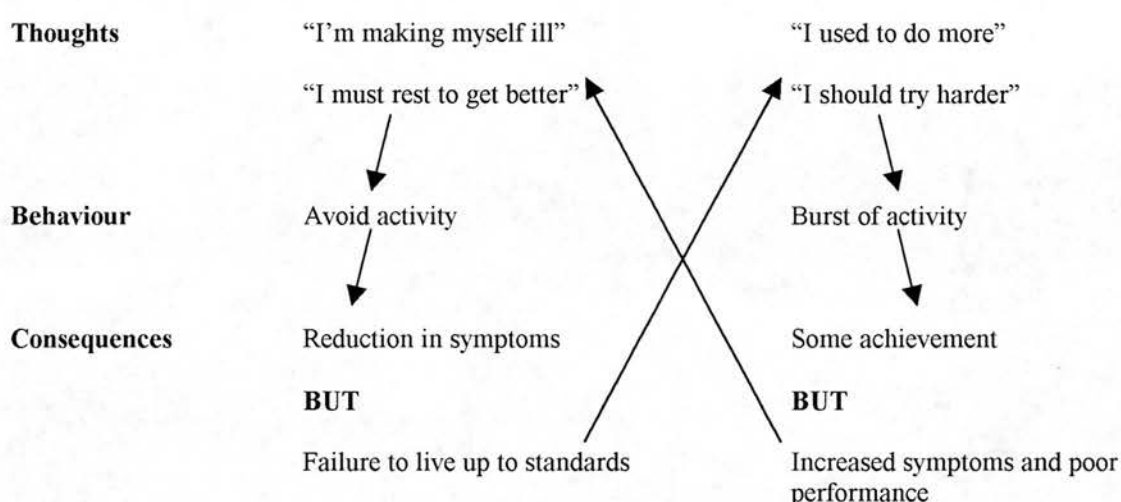
Fig 2.0 Theoretical Cognitive Model of Aetiology of CFS (Surawy et al 1995)



The model further proposes that once fatigue is established, cognitive, behavioural, emotional and physical factors may act to perpetuate it. It is suggested that the symptoms of fatigue, poor concentration and muscle pain results from physical changes accompanying emotional distress and inactivity. Symptoms are regarded as indicating the presence of a disease process, anything exacerbating the symptoms tends to be avoided leading to de-conditioning which in the longer term perpetuates the intolerance of physical and mental activity. An opposing motivation to

avoidance is the desire to perform and meet responsibilities so that episodic attempts to perform at pre-morbid levels fail and worsen the symptoms. A vicious cycle alternating between frustrated effort and ineffectual rest (The rest-burst Cycle) is seen as maintaining the symptoms and keeping patients trapped in chronic illness. This cycle is illustrated in Fig. 3.0.

Fig 3.0 The Perpetuation of CFS (Surawy et al 1995)



Studies, which have examined prognosis in CFS, have lent further support to the theory that psychological factors are of primary importance in the maintenance of CFS and determining outcome (Sharpe, Hawton, Seagroatt & Pasvol, 1992; Wilson et al, 1994; Clark, Katon, Russo, Kith, Sintay, & Buchwald, 1995). A further study found a relationship between high self-efficacy and recovery (Vercoulen, Swanink, Fennis et al, 1995). Attribution of illness to viral infection was associated with poor outcome in three studies (Sharpe et al, 1992; Vercoulen et al, 1995; Wilson et al, 1994). It has been suggested that this attribution may be associated with many other beliefs and lead to life-style and behavioural changes, which have been demonstrated

to indicate poor outcome. There is also evidence that the tendency to catastrophise is associated with more disability (Petrie, Moss-Morris, & Weinman, 1994) which suggests that symptom interpretation is a powerful influence on disability. The link between poor outcome and depression/attributional style is a common finding in many other physical illnesses including myocardial infarction (Ladwig, Roll, Breithardt, et al, 1994) and back pain (Burton, Tillotson, Main, & Hollis, 1995)

1.7.3 Depression as a result of chronic fatigue syndrome

An alternative possible explanation for the relationship between CFS and depression is that depression may be in effect a result of CFS. Two principal theoretical mechanisms have been proposed to explain such an effect.

Organic Hypothesis

An organic mental disorder (OMS) is a mood disturbance in which a specific organic factor can be implicated as the aetiological agent. A number of toxic and metabolic factors have been implicated in OMS, including; medication, endocrine disorders, structural disease of the central nervous system and infectious diseases including viral illness (Lishman, 1987).

Abbey and Garfinkel (1991) assert that it is a well recognised clinical finding that viral illness may produce neurological diseases such as encephalitis and meningitis and that there may be sequelae of these diseases including OMS and personality changes (Cadet & Lohr, 1987; Jefferson & Marshall; 1981, Lishman, 1987). All viruses that have been implicated in CFS have been known to produce

psychiatric symptoms (Cadet & Lohr, 1987; Lishman, 1987). Depression has been found to co-occur with infectious mononucleosis (Cadie, Nye & Storey, 1976; Hendler, 1987) and following infection with the Herpes virus (Greenwood, 1987). The patho-physiological mechanism by which CFS could produce an OMS is unclear. Lishman (1987) suggested that these diseases may either result from direct action within the central nervous system or may occur secondary to autoimmune or hypersensitivity reactions to the presence of the virus outside the central nervous system. In addition to this, it has been suggested that an OMS could occur as the result of the presence of circulating interferon and other cytokinines induced by viral infection (Hickie et al, 1990; Jones & Miller, 1987). Supporting this hypothesis there have been several reports of the therapeutic use of interferon and lymphokines producing symptoms similar to CFS (Denikoff, Rubinow, Papa, Simpson, et al, 1987; Smedley, Katrak, Sikora & Wheeler, 1983).

People who use the term 'ME' often refer to psychological symptoms from depression to memory loss/cognitive impairment as 'encephalic'. Neuropsychological studies involving CFS patients have produced mixed findings. Some studies have found normal to near normal cognitive status in CFS patients or could account for mild neuropsychological deficits on the basis of severity of depression (Altay, Toner, Booker, et al, 1990; Cope, Pernet, Kendall & David, 1995; Krupp, Sliwinski, Doscher et al, 1992- cited in Grafman, 1994). Other studies have found mainly deficits in memory (Riccio, Thompson, Wilson et al, 1992; Sandman, Barron, Nackoul, et al, 1993) and attention/concentration (Smith, 1992). In some studies correlations have been found between the severity of cognitive and mood state complaints and objective testing has not substantiated the range and severity of the

cognitive complaints reported by CFS patients (Grafman, 1994). More recent neuro-imaging studies have found a substantially increased number of defects in chronic fatigue syndrome patients compared with normal controls but no difference between CFS and depressed controls (Schwartz, Komaroff & Garada, 1994). Another study found brainstem blood perfusion was significantly reduced in CFS compared with controls, with depressed patients showing intermediate values (Costa, Tannock & Brostoff, 1995). These results however, await replication.

Overall, the research evidence relating to the role of viruses in the development of CFS would not appear to support the organic hypothesis as a complete explanation for depression in CFS although it may explain depression in some individuals where a virus is clearly implicated in the development of CFS. The finding of pre-morbid psychiatric histories in many patients would also appear to go against this explanation, as it is suggestive of a pre-existing vulnerability to depression not associated with viral infection, but probably linked to increased vulnerability to the development of CFS.

Adjustment Disorder; The Psychological Response to a Disabling Illness

It is well established that depression can be an understandable consequence of physical illness. Depressive reactions occurring in the wake of chronic physical illness have been alternatively described as de-moralisation (Derogatis & Wise, 1989) or despondency (Cassem, 1987). Adjustment disorders (DSM III-R) consist of mild transitory symptoms responding to patterns of remission and relapse in the underlying condition, and 'dysthymic' reactions where the disorder of mood is unremitting, but where valid indicators of major depressive disorder (active suicidal

intent, loss of appetite/desire, guilt and anhedonia) are absent. Snaith (1987) attests to the primary role of anhedonia (pleasure/responsiveness) in successfully discriminating between primary depressive and emotionally adaptive responses to physical illness.

The rate of psychiatric disorder however is higher in CFS than in other medical conditions with a similar degree of disability (Wessely & Powell, 1989; Katon et al, 1991; Wood et al, 1991). It has been postulated that diagnostic delay, uncertainty and scepticism regarding CFS may be at the root of their psychological disturbance (Abbey & Garfinkel, 1991; David, 1991). However assessments of neurological patients lacking a definite diagnosis do not show raised levels of psychiatric symptoms (Bridges & Goldberg, 1984).

Powell, Dolan & Wessely (1990) undertook a fine-grained analysis of the depressive symptoms in post-viral fatigue syndrome (PVFS) and control subjects. They found items concerning loss of pleasure, feelings of guilt and low self-esteem featured less prominently in the PVFS group. This group attributed their illness almost exclusively to a viral cause and this was interpreted as indicating that physical expressions of low mood relate to an individual's cognitive style and afford protection from pathological guilt (defensive hypothesis for somatisation). However another interpretation is that the depressive symptoms in the PVFS group represented an adjustment reaction. A similar attributional bias was detected in Hickie's study (1990) and the CFS patients in the study did not appear to demonstrate personality features characteristic of somatisation disorder. In addition 30 to 50 per cent of the CFS subjects failed to meet criteria for affective disorder and depressive symptoms

were of a lower clinical severity compared with patients receiving treatment for depressive disorder. As stated previously this study recruited chronic fatigue syndrome subjects from a neurological population and its findings may therefore be partly attributable to a sampling bias. In another study (Proctor, 1991) CFS patients were compared with a group of patients with rheumatoid arthritis, chosen as a comparatively disabling illness with a reported risk of secondary 'reactive' depressive disorder. Psychiatric symptoms were barely distinguishable between the two groups, supporting the hypothesis of reactivity in accounting for the CFS depressive sequelae. Consistent with the features associated with secondary reactive disorder, CFS depression was found to remain hedonic, coexisting with neurotic and somatic features and infrequently associated with attitudes of guilt or self-depreciation. A low rate of pre-illness psychiatric disorder was found in the CFS group (20%), a rate not significantly different to that found in the rheumatoid arthritis group and closely matching prevalence rates found in community surveys. This was interpreted as providing evidence against the 'depression-vulnerability' hypothesis.

It has been suggested that there may be a heightened susceptibility to depression in the population with chronic fatigue syndrome, given the clinical descriptions of personality characteristics reported for CFS patients; achievement orientation, goal-driven, exceptionally active (Salit, 1985, Surawy et al, 1995). Beck (1983) described depressive vulnerability in individuals whose self-esteem and pleasure are contingent upon achievement. In such individuals it would be predictable that incapacitation secondary to viral illness resulting in the loss of goal-orientated activities would render them susceptible to depression. This explanation

of adjustment disorder in CFS patients contrasts with the cognitive-behavioural model of CFS, where the same personality characteristics and underlying dysfunctional assumptions lead to a state of chronic exhaustion and demoralisation in response to stress and illness and play a part in the perpetuation of chronic fatigue once it is established. According to the cognitive behavioural model, CFS sufferers may admit feeling depressed as a result of their physical symptoms but do not accept depression or psychological factors as a possible cause of their difficulties.

1.7.4 CFS and Major depressive disorder as Covariates

A slight variation on the organic hypothesis is the suggestion that CFS and major depressive disorder may be covariate phenomena that arise from some other, presently unknown, underlying patho-physiological process (Abbey & Garfinkel, 1991; Hotopf & Wessely, 1997). One hypothesis suggests that a viral infectious toxin could produce the symptoms of CFS through central and/or peripheral mechanisms and the symptoms of major depressive disorder through involvement of the CFS. However, as for the organic hypothesis, the research evidence relating to the role of viruses in the development of CFS would not appear to support such an explanation.

1.7.5 MDD as an Artefactual Diagnosis

This hypothesis suggests that the finding of a high prevalence of major depressive disorder in CFS patients is the result of symptom overlap in CFS and MDE, for example; sleep disturbance, fatigue and impaired concentration. It is suggested that

reactive low mood in addition to such symptoms would meet criteria for major depressive disorder. However, a number of researchers have excluded fatigue as a diagnostic symptom of depression in their analyses (Gold et al, 1990, Katon et al, 1991; Wessely & Powell, 1989) without it affecting their results. In one study (Kruesi et al, 1989) diagnosis of major depressive disorder was made solely on the basis of those symptoms the patients did not attribute to CFS and that had not occurred exclusively within the context within his or her illness with CFS. The data were then reanalysed using every symptom, including those attributed to CFS. The second analysis yielded only one more case of major depressive disorder. Overall research evidence would not appear to support this theory although Abbey and Garfinkel (1991) concluded that further systematic study is required to adequately address this hypothesis.

1.8 INTRODUCTION TO CURRENT STUDY

As can be seen from the preceding review of the literature that there are a considerable number of theories relating to the aetiology of CFS and to the relationship between CFS and depression. The literature can leave the reader feeling confused, perhaps reflecting the current limited understanding that exists in relation to this controversial condition, and the politics which surround it. Overall, the evidence appears to suggest that CFS is a heterogeneous disorder of complex aetiology, probably consisting of a number of different categories of the disorder or sub-types. Many of the theories discussed in this literature review appear to overlap with each other and most recognise a complex interaction between biochemical mechanisms, immunocompetence, and psychological processes, involving integrated bodily systems. The exact nature of these interactions is not fully understood and

provides scope for potentially fruitful future research. It would seem likely that the various aetiological theories for CFS are not mutually exclusive, and that different aetiological and maintaining factors operate at different stages of the disorder and in different combinations in different categories of CFS. Similarly, with regard to the different hypotheses for the relationship between CFS and depression, it seems probable that each may be valid at different stages of the disorder and may vary according to category. Further research is required in order to validate syndromal sub-types and differentiate between different aetiological pathways.

The current study was an attempt to further explore the relationship between CFS and depression and examine some of the theories pertaining to this relationship. Two clinical samples were compared: patients with a diagnosis of CFS (Oxford Criteria) and patients with a diagnosis of major depressive disorder or dysthymia (DSM 1V criteria). It was envisaged that patients with both diagnoses (depression and CFS), would form a third group for the purpose of analysis. In keeping with the view of CFS as a complex disorder and the assumption that hypotheses relating to the causation of CFS are not mutually exclusive, this study aimed to examine the plausibility of various hypotheses rather than find a definitive aetiological theory for CFS or sole explanation for its relationship with depression. A number of theories were examined and the main experimental hypotheses were as follows: -

- 1.0 The view of CFS as a heterogeneous disorder would be supported by the finding of subgroups of CFS patients, distinguished by the presence or absence of concurrent depressive disorder and psychological distress.

- 2.0 In support of the depression-vulnerability hypothesis, the CFS group would be found to exhibit more neuroticism and a higher prevalence of premorbid depression than the general population. However, the theory of CFS as a masked form of depression would not be supported by the finding of less neuroticism in the CFS group than the depressed group, with most neuroticism in the CFS group being accounted for by those subjects with concurrent depression.
- 3.0 The Cognitive Behavioural Model of chronic fatigue syndrome and multi-factorial Models which suggest a typical pre-morbid personality in CFS: achievement driven, high personal standards, hard working and extremely active, would be supported by the finding of significantly higher conscientiousness in the CFS compared with the depressed group and test norms
- 4.0 With regard to the theory that the physical symptoms of CFS reflect somatisation of psychological distress and assuming a psychodynamic view of somatisation, it would be expected that the families of origin of CFS group would share a greater number of features, which have been associated with somatising families (Garraida, 1992). It was predicted that this theory would not be supported and the CFS group would not differ significantly from the depressed group and test norms on dimensions of: cohesiveness, expressiveness and independence
- 5.0 It was predicted that family beliefs, which fit with the pre-morbid personality features of CFS patients proposed by multi-factorial and cognitive behavioural

models of chronic fatigue syndrome would be found to be significantly more prevalent in the CFS sample. Specifically, it was predicted that the CFS group would score higher on achievement-orientation and lower on active-recreational orientation than both the depressed group and test norms

In addition to these main hypotheses, other minor hypotheses considered were as follows:

- (1) It was predicted that chronic levels of fatigue would be found in both depressed and chronic fatigue syndrome groups.
- (2) A positive correlation would be found between emotional distress (HADS scores) and severity of fatigue.
- (3) The CFS and depressed groups would be found to differ significantly in respect of their attributions for symptoms. It was predicted that the CFS patients (depressed and non-depressed) would attribute their symptoms more to external causes (illness), whereas the depressed group would attribute their symptoms more to internal causes.

2 METHOD

2.1 DESIGN

Two groups of patients: CFS and depression were compared using questionnaire measures of: psychological distress, fatigue, personality factors, and dimensions of family functioning. The CFS group was further subdivided into two groups: CFS/only and CFS/ depression for the purpose of comparison.

2.2 THE SAMPLES

Two clinical samples were compared. The first sample comprised 35 patients aged 16-65 years with a diagnosis of chronic fatigue syndrome (Oxford Criteria, Sharpe et al, 1991). Most of the sample (N=28) comprised of patients attending an outpatient chronic fatigue syndrome clinic within a hospital infectious diseases unit. Of these patients, 25 were approached personally at the clinic and 17 returned questionnaires. A further 30 patients were approached by letter and 11 returned questionnaires. Overall the response rate for patients attending the infectious diseases clinic was 51%.

The remainder of the sample (N=7) comprised of patients attending for outpatient treatment (mainly cognitive-behaviour therapy) at various psychiatry/clinical psychology outpatient clinics. Information pertaining to response rate for this group was not available.

Within this sample a sub-sample (N=19) of patients with a concurrent diagnosis of major depressive disorder (MDD) were identified with the purpose of data analysis. Patients were allocated to this group on the basis of a diagnosis of

depression having being recorded in the case notes and subsequent discussion with the clinician involved to clarify this diagnosis. Clinical diagnosis of depression was further checked by application of a checklist of diagnostic criteria for major depressive disorder (DSM-1V) to the information available in patient case notes.

The second sample comprised 33 patients aged 16 to 65 years with a diagnosis of unipolar major depressive disorder (DSM-1V) or dysthymia attending a range of outpatient psychiatry/clinical psychology services for assessment and treatment. A substantial proportion of the sample (N=24) was drawn from patients attending a university student psychiatric service, most of whom were young adult undergraduates. Of 30 questionnaire packs given out to this group, 24 were returned, giving a response rate of 80% for this group. Information pertaining to response rates for depressed subjects recruited from other outpatient clinics was not available.

Exclusion criteria for this sample included; diagnosis of bipolar illness, concurrent diagnosis of eating disorders and substance use disorders, presence of psychotic symptoms, recent treatment with ECT, and the presence of another significant disabling physical condition. Patients with a concurrent diagnosis of anxiety disorders were included in the sample when psychiatric opinion suggested they were clearly secondary to major depressive disorder.

2.3 MEASURES

2.3.1 The Hospital Anxiety and Depression scale (HADS)

This scale was administered as a self-report measure of anxiety and depression (Zigmond and Snaith, 1983). It has demonstrated reliability and validity as a

screening tool, a rating scale and as an instrument for assessing clinical caseness among general medical patients and community samples (Aylard, McKenna, and Snaith, 1987). When compared with the clinical interview schedule (CIS), the sensitivity and specificity of the HADS were: 72.3% and 77.1% respectively and the reliability was 0.74 (Lewis and Wessley, 1990). This scale was chosen as a measure of anxiety and depression in this study because it avoids questions relating to systemic symptoms of depression, which may overlap, with symptoms of physical illness and in the case of this study symptoms of chronic fatigue syndrome. In this study the HADS was used as a measure of emotional distress and to determine current clinical caseness. Scoring of ten and above on either sub-scale (range 0 – 21) was taken stringent criteria for cases (8 to 10 = border line).

2.3.2 The Chalder Fatigue Scale

This eleven item self-rating scale was used to measure the severity of fatigue. Factor analysis has supported a two-factor solution: physical and mental fatigue (Chalder, Berelowitz, Pawlikowska, 1993). The scale has been found to be both reliable and valid, with a high degree of internal consistency. For all items (Cronbachs alpha 0.89), for physical fatigue (0.845), and for mental fatigue (0.821). The validation coefficients for the fatigue scale were: sensitivity 75.5 and specificity 74.5 (Chalder et al, 1993).

A likert scoring system was used to score the questionnaires with values of 0-1-2-3 assigned to the response categories giving a total score range of between 1 and 33. The higher the score the more fatigued the respondent.

The questionnaire included five further items. (Chalder, 1998). Two of these related to muscle pain and two forced choice questions related to duration of tiredness and percentage of time spent feeling tired. Finally subjects were asked an open question about the cause of their tiredness.

2.3.3 The Family Environment Scale (FES)

A modified version of the family environment scale (Moos, 1974) was used in this study as a measure of the social-environmental characteristics of the subject's families (Family functioning). This ninety item self-report measure comprises ten sub-scales, which assess three underlying domains; the relationship dimensions, the personal growth dimensions, and systems maintenance dimensions. The relationship dimensions are measured by the cohesion, expressiveness, and conflict sub-scales. The personal growth or goal orientation dimensions are measured by the independence, achievement-orientation, intellectual-cultural orientation, active-recreational and moral-religious emphasis sub-scales. The systems maintenance dimensions are measured by the organisation and control sub-scales. The FES (Form R) was modified slightly for use in the study. Subjects were instructed to complete the questionnaire retrospectively to describe their family of origin rather than within any current family. The questionnaire was worded in the past tense and subject responses (true/false) were recorded on the questionnaire next to the item rather than on a separate response form. The language of two items was modified very slightly to make them more suitable for a Scottish population.

Analysis of normative data on the FES (form R) sub-scales found that the form R results were representative of a range of normal families (Moos and Moos,

1981). As expected, when compared to normal families, the stressed families were lower on cohesion, expressiveness, independence, intellectual and recreational orientation and higher on conflict and control (Moos and Moos, 1981). The internal consistencies of each of the ten FES sub-scales are all in acceptable range, Cronbach's alpha ranging from a low of 0.61 for Independence and 0.78 for Cohesion, as are the test retest reliabilities, ranging from a correlation of 0.68 for independence and 0.86 for cohesion (Moos and Moos, 1981). The Family environment scale can be used to describe or compare the social environments of families and has been employed in over one hundred research projects (Moos and Moos, 1981).

2.3.4 The NEO Five Factor Inventory (NEO-FFI)

The NEO FFI (Costa & McCrae, 1991) is a sixty-item version of the longer (240 items) NEO Personality Inventory Revised (NEO PI-R) (Costa and McCrae, 1992). The NEO PIR was developed to operationalise the five-factor model of personality, which has developed over the past forty years (Digman, 1990). The five factors represent the most basic dimensions underlying the traits identified in both natural languages and Psychological questionnaires. The NEO FFI provides a measure of the five broad domains or dimensions of personality; Neuroticism (N) Extroversion (E) Openness (O) agreeableness (A) and conscientiousness (C) whereas the longer NEO PIR provides a more fine grained description of personality in terms of the inter correlated traits, termed "facets" which make up the five domains.

The NEO PI-R was developed from a substantive body of research and there is good evidence on scale validity, reliability and stability and construct validity for the scale.

The Cronbach's alpha for the domains are: N (0.92), E (0.89), O (0.87), A, (0.86), and C (0.90) (Costa, McCrae & Dye, 1991) reflecting a high degree of internal consistency. The three month retest reliability of the NEO-FFI scales in a college sample were: coefficients .79, .79, .80, .75, and .83 for the N, E, O, A, and C domains respectively ($p < .001$) (Costa & McCrae, 1992). Correlations between the NEO-PI and two other instruments which operationalise the five-factor model: the California Q set (Block, 1961) and The Hogan Personality Inventory (Hogan, 1986) have supported the construct validity of the NEO-PI domains and factors (Goldberg, 1989- cited in Costa & McCrae, 1992; McCrae Costa & Busch, 1986). The finding that patients in psychotherapy score high on N (Miller, 1991) and that drug abusers score low on A and C (Brooner et al, 1991- cited in Costa & McCrae, 1992) provide some evidence of criterion group validity for the NEO-PI scales

Although devised as a measure of normal personality traits through thorough research and voluntary samples, The NEO PI has been used widely for assessment purposes in clinical settings. (Miller, 1991) showed that neuroticism was associated with the presence of DSM III-R diagnosable disorders and found that both neuroticism and conscientiousness were significant independent predictors of therapeutic outcome. It has been suggested (Widiger and Trull, 1993) that several axis one disorders, such as dysthymia, are in fact trait dispositions to experience mood and that neuroticism may be related to a host of axis-one disorders. Links between the five-factor model and the eleven axis-two disorders have been documented in several research contexts (Costa & Widiger, 1992). Of relevance to the current research, the NEO PI-R has been used in behavioural medicine for the assessment of somatic complaints, for which it has been proposed that the most

prominent determinants are objective health status and neuroticism (Costa & McCrae, 1985a, 1987a).

The NEO- FFI was developed from the NEO PI-R (Costa & McCrae, 1992) using factor analytic techniques. Research examining validity for the shorter version suggests that the NEO- FFI is not equivalent to the full domain scales of the NEO-PIR. On average the shorter scales appear to account 85 per cent as much variance in the convergent criteria as do factor scores, which may be considered as an acceptable trade off for speed and convenience.

The Five Factors

Neuroticism- This domain contrasts emotional stability or adjustment with maladjustment or neuroticism. The general tendency to experience negative effects such as fear, sadness, embarrassment, anger, guilt and disgust is the core of the neuroticism domain. In addition, individuals high on N are also prone to have irrational ideas, to be less able to control their impulses and cope more poorly than others with stress. Patients traditionally diagnosed with neurosis generally score high on measures of N (Eysenck & Eysenck, 1964).

Conscientiousness- This domain is concerned with self-control, both the ability to resist impulses and manage desires as well as more active processes of planning and organisation in carrying out tasks. The conscientious individual is purposeful, strong willed and determined. This domain has been described as “will to achieve”. On the positive side high conscientiousness is associated with academic and occupational achievement and on the negative side, competitive workaholic behaviour.

Extroversion- This domain is primarily a dimension of interpersonal tendencies including facets of sociability, gregariousness, assertiveness, excitement seeking and positive emotions. An individual scoring high on E will generally be sociable, cheerful, upbeat, energetic and optimistic.

Agreeableness- This domain is also a dimension primarily of inter-personal tendencies. The agreeable person is fundamentally altruistic, sympathetic to others and eager to help them. In return the agreeable individual believes that others will be equally helpful in return. By contrast the antagonistic disagreeable person is egocentric, sceptical of others intentions and competitive rather than co-operative.

Openness- The elements of openness include; active imagination, aesthetic sensitivity, attentiveness to inner feelings, preference for variety, intellectual curiosity, and independence of judgement. Alternative formulations of the five-factor model often labelled this factor “intellect” and openness is especially related to aspects of intelligence, such as divergent thinking that contribute to creativity (McCrae, 1987). Individuals who score low on openness tend to be conventional in behaviour and conservative in outlook. They prefer the familiar to the novel and their emotional responses are somewhat muted. Open individuals are by contrast unconventional, willing to question authority, and prepared to entertain new ethical, social, and political ideas.

2.4 PROCEDURE

CFS Sample

Suitable patients that were attending a chronic fatigue syndrome outpatient clinic at an infectious diseases unit for second or subsequent appointments were identified by their consultant and invited to meet the researcher to discuss participation in the research. At this meeting the main research aims and requirements were explained and consent was obtained. Subjects who agreed to participate were given a questionnaire pack containing the four questionnaire measures and a research information sheet to take away for completion and return in a stamped address envelope provided.

At a later stage of the research, due to the low numbers of suitable CFS patients passing through the CFS clinic, a smaller number of CFS patients attending the clinic infrequently for follow-up appointments were contacted by letter and invited to participate in the research. A pack containing the four questionnaire measures and a research information sheet was sent, with this letter, for completion and return in an enclosed stamped addressed envelope.

A small number of CFS patients attending clinical psychology and psychiatry outpatient clinics were informed of the research by their clinician and invited to participate. Consent was obtained and willing participants were given the research pack containing the questionnaires and an information sheet to take home for completion and return.

Depressed Group

Suitable depressed patients attending a university psychiatry outpatient clinic were identified by their consultant and invited to meet the researcher to discuss participation in the research. At this meeting the research aims and requirements were explained and consent was obtained. Willing participants were given a pack containing the research questionnaires and an information sheet to take away for completion and return in a stamped addressed envelope provided.

The remaining patients in this group were informed of the research by their clinician and invited to participate. Consent was obtained from willing patients who were then given the research pack to take home for completion and return.

All Subjects

The psychiatric/medical notes of all participants were examined for the following information:

CFS Patients

1. Documented diagnosis of the chronic fatigue syndrome.
2. Evidence to support the concurrent diagnosis of psychiatric disorder.
3. Evidence of premorbid psychiatric history
4. Patient beliefs relating to the causation of their illness.

Depressed Patients

1. Documented diagnosis of major depressive disorder
2. Information pertaining to inclusion/exclusion criteria.

2.5 ANALYSIS

All analyses were performed using SPSS (statistical package for social sciences). The first stage of the analysis provided descriptive data on the subjects in each sample. The subsequent analysis was concerned with the testing of hypotheses described earlier.

3 RESULTS

Sixty-eight subjects were recruited for the study. Analyses were performed on two main groups: CFS (N = 35) and depression (N = 33). The CFS group was divided into two sub-groups for the purpose of further analyses: CFS/no depression and CFS with depression.

3.1 DEMOGRAPHIC DATA

Data relating to age and gender are summarised in table 3.1.

Table 3.1 Demographic Data

	MAIN GROUPS	
	CFS (N = 35)	Depression (N = 33)
Sex m/f	9/26	11/22
Age (mean (95% confidence interval)	39.46 (35.65 - 43.27)	28.67 (24.50 - 32.83)
	Sub Groups	
	CFS/no Depression N = 16	CFS + Depression n = 19
Sex m/f	4/12	5/14
Age (mean) (95% confidence interval)	38.81 (33.00 - 44.62)	40.0 (34.44 - 45.56)

The depressed group was significantly younger than the CFS group, reflecting the over-representation of University Undergraduates in the depressed sample ($t = 3.895$, $df = 66$, $p < 0.001$).

Females predominated in all groups, which were well matched on gender.

The possibility that age may have contributed to differences in the main outcome variables in this study necessitated its inclusion as a covariate in some of the subsequent analyses.

3.2 CURRENT PSYCHIATRIC STATUS

3.2.1 Depression

Overall, 54% of the CFS group were categorised as suffering from a co-morbid depressive disorder. This categorisation was made on the basis of clinician diagnosis and application of a checklist of diagnostic criteria for MDD (DSM-IV) to case note information. 11.4% (n = 4) of the CFS group satisfied HADS criteria for caseness, depressive disorder and a further 28.6% satisfied HADS criteria for caseness, anxiety and depression.

3.2.2 Anxiety

Overall 37% of the CFS group were categorised as suffering from a co-morbid anxiety disorder. This categorisation was made on the basis of clinician diagnosis recorded in the subjects' case notes. 25% of the CFS group satisfied HADS criteria for caseness, anxiety disorder only.

3.2.3 Psychiatric Disorder

Overall 71% of the CFS group were categorised as suffering from a psychiatric disorder.

3.3 PRE-MORBID PSYCHIATRIC DISORDER

3.3.1 Pre-morbid affective disorder

The estimated prevalence of pre-morbid affective disorder in the CFS group was 31.4%

3.3.2 Pre-morbid psychiatric disorder

The estimated prevalence of pre-morbid psychiatric disorder in the CFS group was 42.0 %.

These estimates were based upon information recorded in subjects' case notes.

3.4 EMOTIONAL DISTRESS - HADS SCORES

3.4.1 Exploratory Data Analysis

HADS scores, including: total and subscale scores, were found to approximate to the normal distribution, for all groups/sub-groups studied, and there were no problems with Kurtosis or skew.

3.4.2 HADS Total Score

Across Main Group Comparisons: CFS and Depression

HADS total scores were significantly higher in the depressed group than the CFS group ($t = 3.35$, $df = 66$, $p < 0.001$). See table 3.42a

Table 3.42a- HADS total scores for main groups: Depressed and CFS

	CATEGORY	N	Mean	Std. Deviation	Std. Error Mean
HAD TOTAL SCORE	DEPRESSED	33	23.6364	6.8457	1.1917
	CFS	35	18.1385	6.6955	1.1317

When this analysis was repeated with age as a covariate, age effects were not found to be significant ($p = 0.47$) and the group effect persisted at the same level of significance ($F = 11.26$, $df = 1,64$, $p < 0.001$), therefore age differences did not account for the differences in HADS total scores across the groups.

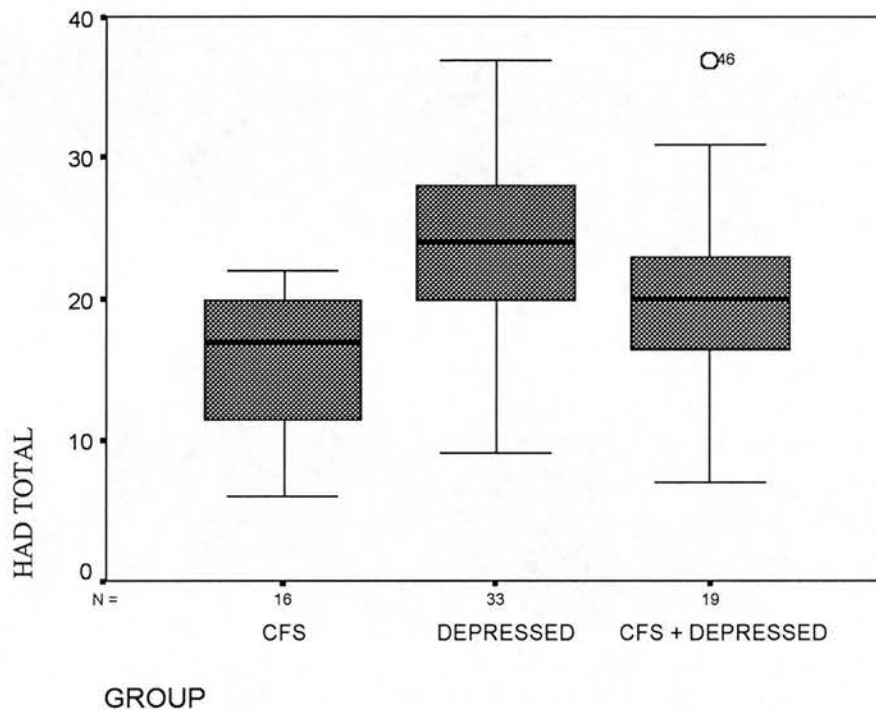
Across Sub-group Comparisons

A one-way ANOVA revealed a significant difference across the sub-groups ($F = 8.6$, $df = 2,65$, $p < 0.001$). See Table 3.42b

Table 3.42b HADS total scores for sub-groups: Depressed, CFS only, and CFS with depression

GROUP	Mean	N	Std. Deviation
CFS	15.365	16	5.0650
DEPRESSED	23.636	33	6.8457
CFS + DEPRESSED	20.473	19	7.1209

Figure 3.42: Boxplot- HADS total scores for subgroups



Pairwise comparisons confirmed that the depressed group had higher HADS total scores than the CFS/no depression group ($p < 0.001$), but not the CFS/depression group.

When this analysis was repeated with age as a covariate, age effects were not found to be significant and the group effect persisted at the same level of significance ($F=8.53$, $df=2,63$, $p<0.001$). Therefore age differences did not account for the differences in HADS total scores across the groups.

Pairwise comparisons (Simple and Helmert contrasts) confirmed a significant group effect with the CFS group scoring significantly lower than both the CFS with depression group and the depressed group.

CFS vs. CFS/depression	p = 0.027
Depression vs. CFS/depression	p = 0.07
CFS vs. CFS/depression and depressed	p = 0.001

The sub-groups of CFS were, therefore, differentiated on the basis of HADS total scores. The CFS/ depression group did not differ significantly from the depressed group on HADS total score.

3.4.3 HADS - Depression Scores

Across Main Group Comparisons : CFS and Depression

HADS - depression scores were significantly higher in the depressed group than the CFS group ($t = 2.00$, $df = 66$, $p = 0.05$). See Table 3.43a

Table 3.43a-HADS depression scores for main groups

	CATEGORY	N	Mean	Std. Deviation	Std. Error Mean
HAD DEPESSION	DEPRESSED	33	10.2727	4.5844	.7980
	CFS	35	8.2857	3.5692	.6033

When this analysis was repeated with age as a covariate, age effects were not significant and the group effect persisted at a higher level of significance ($F = 11.26$, $df = 1, 64$, $p = 0.025$)

The number of subjects satisfying HADS criteria for caseness; depression (see table 3.34b), did not differ significantly across the 2 groups ($X^2 = 2.86$, $df = 1$, $p = 0.09$)

Table 3.43b.: HADS caseness ;depression for the two main groups

		CATEGORY	
		DEPRESSED	CFS
HADS depression caseness	not case	13	21
	case	20	14

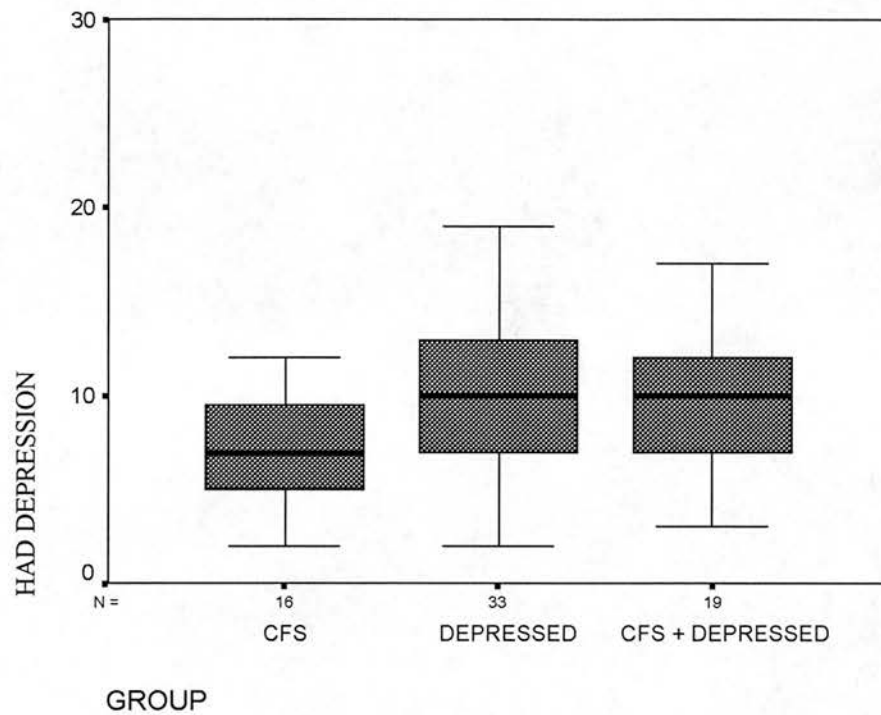
Across Sub-group Comparisons: CFS/no depression, CFS/depression, Depression

A one-way ANOVA revealed a significant difference across these groups ($F = 3.73$, $df = 2,65$, $p = 0.03$).See Table 3.43c.

Table 3.43c: HADS depression scores for subgroups

GROUP	Mean	N	Std. Dev
CFS	6.937	16	3.1085
DEPRESSED	10.27	33	4.5844
CFS+ DEPRESSED	9.421	19	3.6104

Figure3.43: Boxplot- HADS depression scores for subgroups



Pairwise comparisons confirmed that the depressed group had significantly higher HADS depression scores than the CFS/no depression group ($p = 0.022$) but not the CFS/ depression group.

When this analysis was repeated with age as a covariate, age effects were not found to be significant ($F = 4.3$, $df = 2,63$, $p = 0.018$) and the group effect persisted at the same level of significance. Therefore age differences did not account for the differences found in HADS depression scores across the groups.

Pairwise comparisons confirmed that the CFS/no depression group had significantly lower HADS depression scores than the depressed group but not

the CFS/depressed group. The CFS/ depression group and the depressed group did not differ significantly on HADS depression scores.

CFS vs. CFS/depression $p = 0.08$,

CFS/depression vs. Depression $p = 0.28$,

CFS vs. CFS/depression + depression $p = 0.01$

The sub-groups of the CFS group were not differentiated by HADS depression scores.

The difference in the number of subjects satisfying HADS criteria for caseness, depression (see table 3.43d) approached significance across the three sub-groups ($X^2 = 5.537$, $df = 2$, $p = 0.063$).

Table 3.43d: HADS caseness, depression for the sub-groups

		GROUP		
		CFS	DEPRESSED	CFS + DEPRESSED
HADS depression caseness	not case	12	13	9
	case	4	20	10

Pairwise comparisons revealed that there was significantly more caseness, depression in the depressed group than the CFS/ only group ($X^2 = 5.47$, $df=1$, $p=0.019$)

All other subgroup comparisons were non-significant.

3.4.4 HADS - Anxiety Scores

Across Main Group Comparisons : CFS and Depression

HADS anxiety scores were significantly greater in the depressed group compared with the CFS group ($t = 3.46$, $df = 66$, $p < 0.001$). See Table 3.44a.

Table 3.44a : HADS anxiety scores for the two main groups

	CATEGORY	N	Mean	Std. Deviation	Std. Error Mean
HADS ANXIETY	DEPRESSED	33	13.3636	3.9196	.6823
	CFS	35	9.8429	4.4271	.7483

When this analysis was repeated with age as a covariate, age effects were not found to be significant ($p = 0.83$) and group effects persisted at a very similar level of significance ($t = 10.22$, $df = 1.64$, $p = 0.002$).

The number of subjects satisfying HADS criteria for 'caseness'; anxiety disorder (see table 3.44b) was significantly greater in the depressed group compared with the CFS group ($X^2 = 5.84$, $df = 1$, $p = 0.016$).

Table 3.44b- HADS caseness; anxiety for the main groups

		CATEGORY	
		DEPRESSED	CFS
HADS anxiety caseness	not case	7	16
	case	26	19

Across Sub-group Comparisons : CFS/no depression, CFS/depression, Depression

A one-way ANOVA revealed a significant difference across these groups ($F = 8.04$, $df = 2,65$, $p < 0.001$). See Table 3.44c

Table 3.44c- HADS anxiety scores for sub-groups

GROUP	Mean	N	Std. Deviation
CFS	8.4063	16	4.2474
DEPRESSED	13.3636	33	3.9196
CFS + DEPRESSED	11.0526	19	4.3137

Pairwise comparisons confirmed that the depressed group had significantly higher HADS anxiety scores than the CFS group but not the CFS/ depression group.

When this analysis was repeated with age as a covariate, HADS - anxiety scores were not found to differ significantly with age.

A covariate ANOVA revealed that HADS - anxiety scores differed significantly across the three groups ($F = 7.07$, $df = 2,63$, $p = 0.002$)

Pairwise comparisons confirmed that the CFS/no depression group had significantly lower HADS - anxiety scores than the depressed group but not the CFS/depressed group.

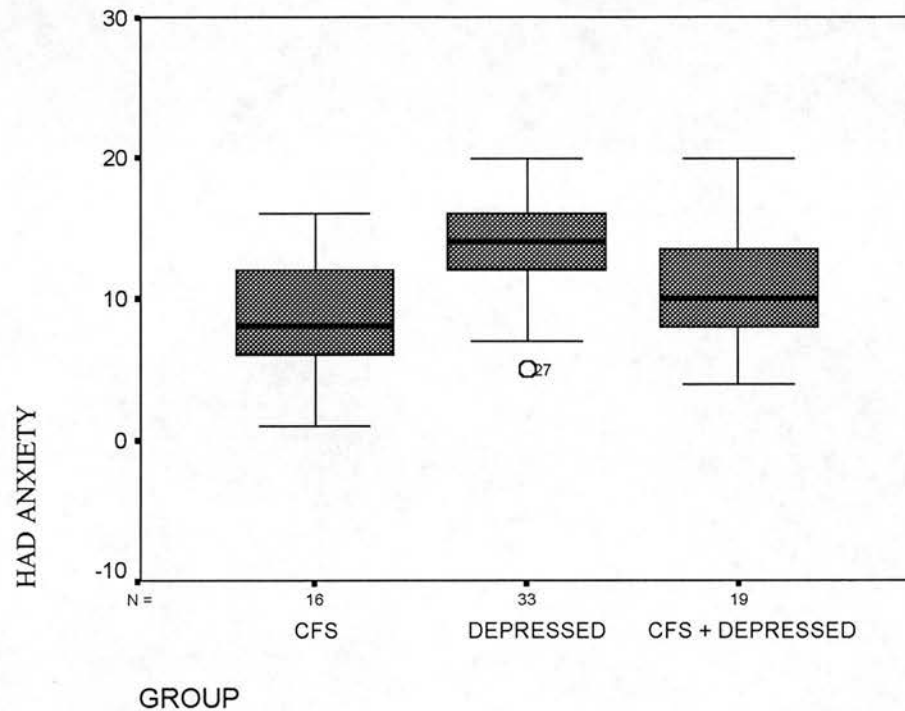
CFS vs. CFS/depression $p = 0.065$

CFS/depression vs. depression $p = 0.07$

CFS vs. CFS/depression and depression $p = 0.002$

The sub-groups of the CFS group were not differentiated by HADS - anxiety scores.

Figure 3.44- Boxplot- HADS anxiety scores for subgroups



The number of subjects satisfying HADS criteria for 'caseness' - anxiety disorder (see table 3.44d) differed significantly across the three groups ($X^2 = 8.95$, $df = 2$, $p = 0.01$).

Pairwise comparisons revealed that there was significantly more caseness; anxiety in the depressed group compared with the CFS/ only group ($X^2 = 6.02$, $df = 1$, $p = 0.014$).

All other sub-group comparisons were non-significant.

Table 3.44d: HADS caseness; anxiety for sub-groups

		GROUP		
		CFS	DEPRESSED	CFS + DEPRESSED
HADS anxiety caseness	not case	9	7	7
	case	7	26	12

3.4.5 HADS 'Caseness' - Anxiety and depression

The number of subjects satisfying HADS criteria for both anxiety and depression (see table 3.45a) was significantly greater in the depressed group ($X^2 = 5.84, df = 1, p = 0.016$).

Table 3.45a- HADS caseness; anxiety and depression for main groups

		CATEGORY	
		DEPRESSED	CFS
anxiety/depression caseness	not case	14	25
	case	19	10

This significant difference remained when the three sub-groups were compared (see table 3.45b) ($X^2 = 8.95, df = 2, p = 0.01$).

Table 3.45b: HADS caseness; anxiety and depression for subgroups

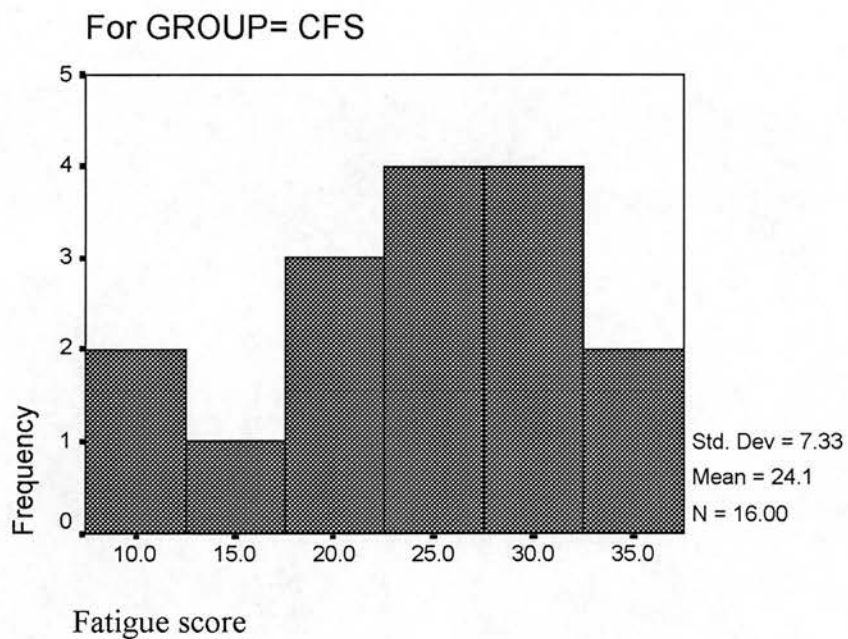
		GROUP		
		CFS	DEPRESSED	CFS + DEPRESSED
anxiety/depression caseness	not case	14	14	11
	case	2	19	8

3.5 FATIGUE SCORES

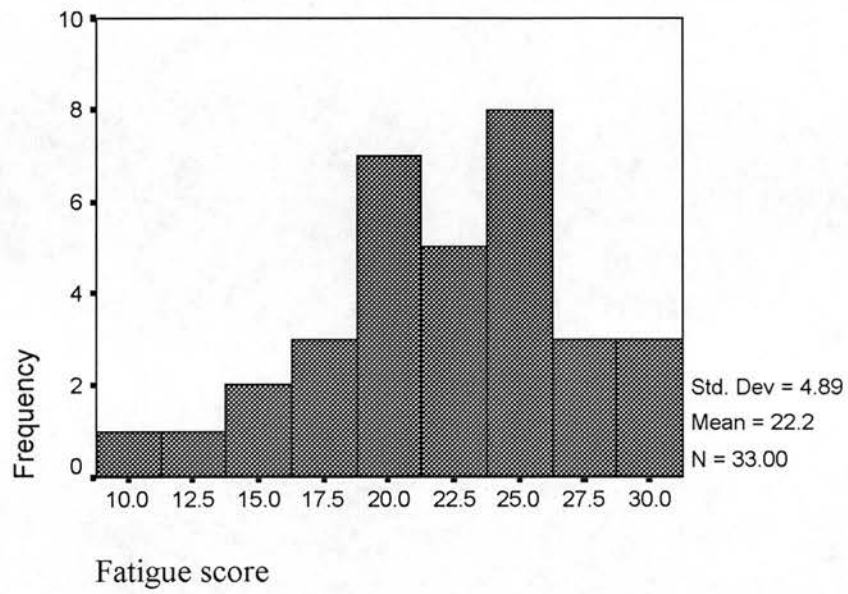
3.5.1 Exploratory data analysis

Fatigue scores were found to approximate to the normal distribution for all groups considered and there were no problems with kurtosis or skew (see Figure 3.51)

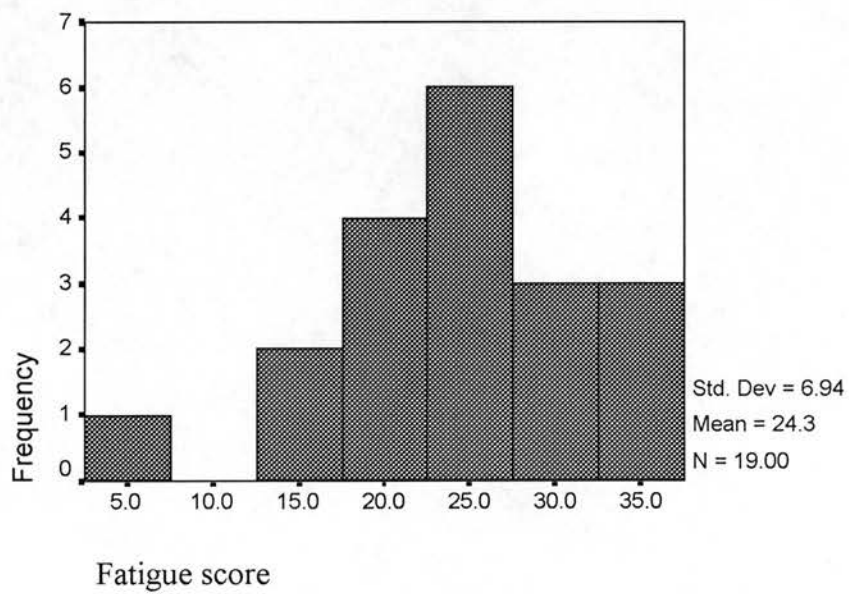
Figure 3.51: Frequency distributions of fatigue scores in the subgroups: CFS / no depression, CFS / depression and depression



For GROUP= DEPRESSED



For GROUP= CFS + DEPRESSED



3.5.2 Across Main Group Comparisons: CFS and Depression

Fatigue scores did not differ significantly across these groups ($t = 1.37$, $df = 66$, $p = 0.174$). See Table 3.52

Table 3.52: Fatigue scores for main groups

	CATEGORY	N	Mean	Std. Deviation	Std. Error Mean
FATIGUE SCORE	DEPRESSED	33	22.1798	4.8925	.8517
	CFS	35	24.2057	7.0159	1.1859

When the groups were compared with age as a covariate, neither age or group effects were significant -

Age ($F = 0.13$, $df = 1, 64$, $p = 0.91$)

Group ($F = 1.63$, $df = 1, 64$, $p = 0.21$)

3.5.3 Across Sub-group Comparisons : CFS/no depression, CFS/depression and Depression

Similarly fatigue scores did not differ significantly across these groups ($F = 0.936$, $df = 2, 65$, $p = 0.398$). See Table 3.53.

Table 3.53: fatigue scores for sub-groups

	Mean	N	Std. Deviation
CFS	24.075	16	7.3346
DEPRESSED	22.179	33	4.8925
CFS + DEPRESSED	24.315	19	6.9366

The groups considered in both comparisons were not differentiated on the basis of fatigue scores.

When this analysis was repeated with age of a covariate, age effects were not found to be significant ($F = 0.013$, $df = 1,63$, $p = 0.9$).

As was found for the univariate analysis, fatigue scores did not differ significantly across the groups ($F = 0.811$, $df = 2,63$, $p = 0.45$).

3.5.4 The Relationship between Fatigue scores and Emotional distress (HADS -total)

The correlation between fatigue scores and HADS - total scores for the entire data set was: Pearson's $r = 0.351$, significant at the 0.01 level, which shows that a significant relationship exists between HADS-total scores and fatigue scores (see Figure 3.54.)

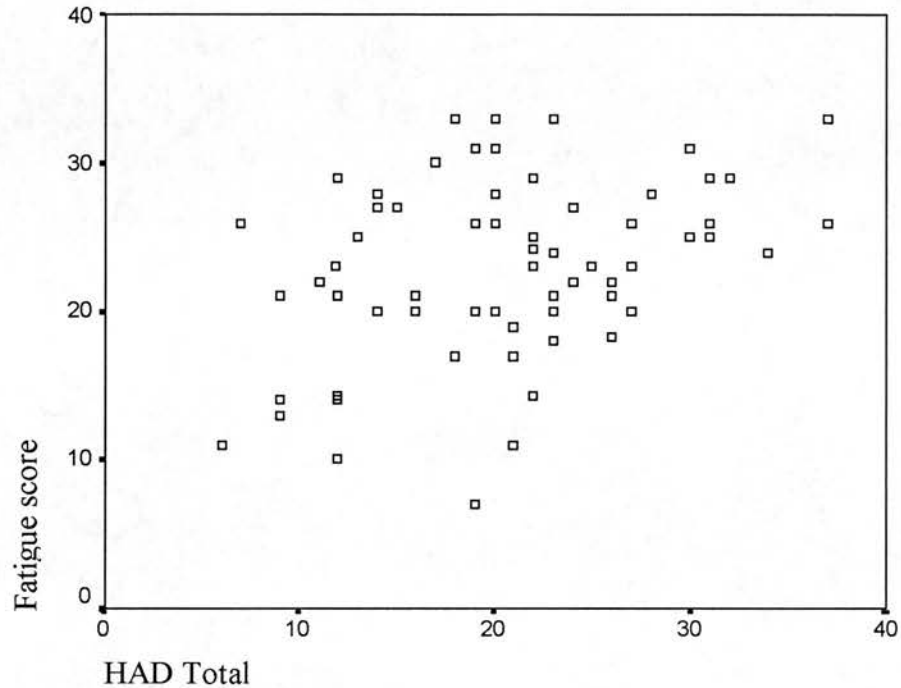
Partialling out the effects of age, the correlation between HADS - total scores and fatigue scores was : Pearson's $r = 0.36$, $df = 65$, $p < 0.01$, which shows age differences do not account for the relationship between HADS-total scores and fatigue scores. For each subgroup the Pearson's correlation coefficients were as follows:-

CFS/only group- $r = 0.48$, $df = 13$, $p = 0.068$

Depression group- $r = 0.53$, $df = 30$, $p < 0.002$

Depression/ CFS group- $r = 0.44$, $df = 16$, $p = 0.065$

Figure 3.54: Scatterplot- fatigue scores against HADS total scores for data set



3.5.5 Attributions for Fatigue

The reasons subjects gave for their fatigue were initially categorised into five groups : physical attribution, psychological attribution, mixed attribution, don't know, or no response and further recategorised, for the purpose of analysis, into three groups: physical attribution, psychological attribution, or other.

Across main-group comparisons : CFS and depression

The number of subjects with a primary physical attribution for their fatigue (see table 5.55a) was significantly greater in the CFS group ($X^2 = 10.73$, $df = 1$, $p < 0.001$).

Table 3.55a: Physical attribution in main groups

		other	physical attribution
CATEGORY	DEPRESSED	32	1
	CFS	23	12

The number of subjects with a primary psychological attribution for their fatigue (see table 3.55b) was significantly greater in the depressed group ($X^2=21.53$ $df = 1$, $p < .001$)

Table 3.55b: Psychological attribution in main groups

		other	psychological attribution
CATEGORY	DEPRESSED	10	23
	CFS	30	5

Across sub-group comparisons

Physical attribution

The number of subjects giving a primary physical attribution for their fatigue did not differ significantly across the subgroups of CFS ($X^2= 3.23$, $df=1$, $p=0.072$).

The number of subjects giving a primary physical attribution for their fatigue was significantly greater in both the CFS and the CFS with depression group compared with the depressed group (see table 3.55c.).

Depression and CFS/only - $X^2 = 15.86$, $df = 1$, $p < 0.001$

Depression and CFS/ depression – $X^2 = 4.5$, $df = 1$ $p = 0.034$

CFS and CFS/ depression groups did not differ significantly in terms of physical attribution. ($X^2 = 1.13$, $df=1$, $p=0.29$).

Table 3.55c: Physical attribution across sub-groups

		Other	physical attribution
GROUP	CFS	8	8
	DEPRESSED	32	1
	CFS + DEPRESSED	15	4

Psychological attribution

The number of subjects giving a primary psychological attribution for their fatigue did not differ significantly across the subgroups of CFS ($X^2 = 2.76$, $df = 1$, $p = 0.096$).

The number of subjects giving a primary psychological attribution for their fatigue was significantly greater in the depressed group compared with both the CFS / only group and the CFS with depression group (see table 3.55d)

Depression and CFS/ only – $X^2 = 8.70$, $df = 1$, $p = 0.003$

Depression and CFS/depression – $X^2 = 20.14$, $df=1$, $p < 0.001$

CFS and CFS/ depression groups did not differ significantly in terms of psychological attribution ($X^2 = 2.13$, $df=1$, $p=0.14$).

Table 3.55d: Psychological attribution across sub-groups

		other	psychological attribution
GROUP	CFS	12	4
	DEPRESSED	10	23
	CFS + DEPRESSED	18	1

3.6 PERSONALITY FACTORS

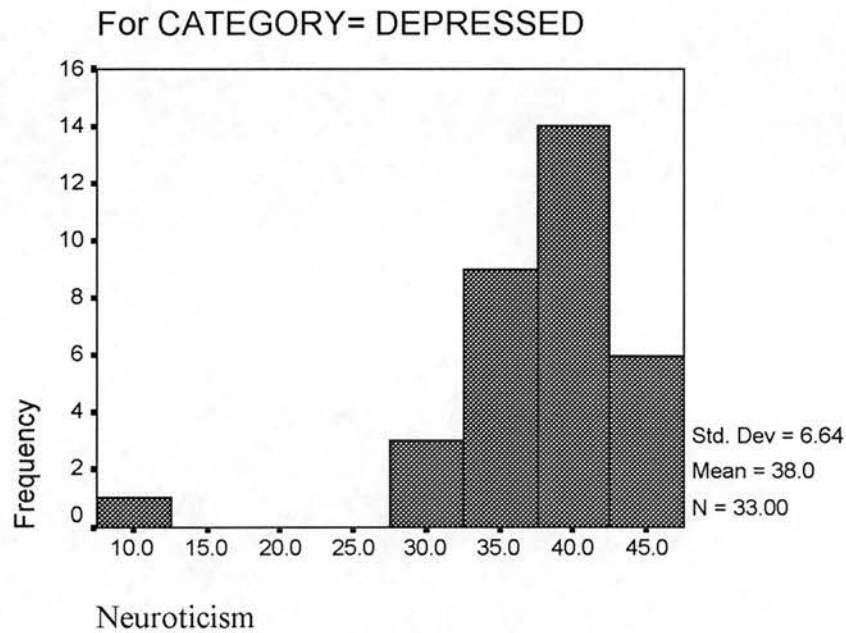
3.6.1 Exploratory data analysis

For all the groups considered in this study, the distributions for all personality dimensions, with the exception of neurosis, approximated to the normal distribution, and there were no problems with Kurtosis or skew.

There was a problem with kurtosis for neuroticism in the depressed group - see Figure 3.61,(kurtosis statistic = 7.603, standard error = 0.798) but it would be expected that a group consisting of psychiatric patients with a diagnosis of MDD would score highly on a measure of 'neuroticism'.

The Kolomogoroff - Smirnoff test of normality for the depressed group was not significant, ($p = 0.15$) and therefore transformation of this variable was not considered necessary.

Figure 3.61: Frequency distribution of neuroticism scores in the depressed group



3.6.2 Comparisons across the two main groups: CES and Depression

Table 3.62: Personality scores for main groups

		Neuroticism	Extraversion	Openness	Agreeable- ness	Conscien- tiousness
DEPRESSED	Mean	37.9697	20.2121	32.8099	29.9515	25.0303
	N	33	33	33	33	33
	Std. Dev.	6.6449	7.0078	5.6923	6.4973	9.6063
CFS	Mean	29.6805	21.4675	28.6078	33.4499	30.4026
	N	35	35	35	35	35
	Std. Dev.	9.1330	6.4409	5.8847	6.6706	7.4979
Total	Mean	33.7032	20.8583	30.6471	31.7521	27.7955
	N	68	68	68	68	68
	Std. Dev.	8.9909	6.7013	6.1258	6.7709	8.9398

Neuroticism

The depressed group scored higher on neuroticism than the CFS group ($t = 4.26$, $df = 66$, $p < 0.001$).

When the groups were compared with age as a covariate, age effects were found to be significant ($F = 6.11$, $df = 1,64$, $p = 0.016$), however the group effect persisted ($F = 8.51$, $df = 1,64$, $p = 0.005$). Age therefore only contributed very slightly to the differences in neuroticism between the two main groups.

Openness to experience

The depressed group scored significantly higher on 'openness to experience' than the CFS group ($t = 2.990$, $df = 66$, $p = 0.004$).

When the groups were compared with age as a covariate, age effects were found to be significant, ($F = 11.65$, $df = 1,64$, $p = 0.001$). The group differences in 'openness to experience' were no longer significant ($F = 2.04$, $df = 1,64$, $p = 0.10$). Age effects therefore accounted for the group differences in 'openness to experience'.

Agreeableness

The CFS group scored significantly higher on agreeableness than the depressed group ($t = 2.19$, $df = 66$, $p = 0.032$).

When the groups were compared with age as a covariate, age effects were not found to be significant ($F = 0.506$, $df = 1,64$, $p = 0.40$). However the differences in agreeableness across the main group was also no longer significant ($F = 2.75$, $df = 1,64$, $p = 0.102$). Age effects therefore account for the group differences found for agreeableness.

Conscientiousness

The CFS group scored significantly higher on conscientiousness than the depressed group ($t = 2.58$, $df = 66$, $p = 0.012$).

When the groups were compared with age as a covariate, age effects were not found to be significant ($F = 2.07$, $df = 1,64$, $p = 0.155$). However the differences in conscientiousness across the main groups, were also no longer significant ($F = 2.97$, $df = 1,64$, $p = 0.09$). Age effects appear to have largely contributed to the group differences in conscientiousness.

Extraversion

The groups did not differ significantly on extraversion. When the groups were compared with age as a covariate, age effects were not found to be significant ($F = 0.003$, $df = 1,64$, $p = 0.955$) and group differences remained non-significant ($F = 0.441$, $df = 1,64$, $p = 0.51$).

3.6.3 Comparisons across Sub-groups: CFS/only, CFS/depression ,depression

Neuroticism

A one-way ANOVA revealed that the three groups differed significantly on 'neuroticism' ($F = 14.64$, $df = 2,65$ $p < 0.001$). Pairwise comparisons confirmed a significant group effect with the CFS/no depression group scoring significantly lower on neuroticism than both the CFS with depression group and the depression group (see Table 3.63a)

Table 3.63a: Neuroticism scores for sub-groups

GROUP	Mean	N	Std. Deviation
CFS	25.5000	16	8.6333
DEPRESSED	37.9697	33	6.6449
CFS + DEPRESSED	33.2010	19	8.1748

When these groups were compared, with age as a covariate, neuroticism scores were found to differ significantly with age ($F = 7.65$, $df = 1,63$, $p = 0.007$). However the group effect remained significant for neuroticism ($F = 10.147$, $df = 2,63$, $p < 0.0001$).

As previously pairwise comparisons (simple and helmet contrasts) found a significant group effect with the CFS/ no depression group scoring significantly lower than the other two groups

(CFS vs. CFS + depressed $p = 0.007$)

Depressed vs. CFS + depressed $p = 0.31$

CFS vs. CFS/depressed + Depressed $p = < 0.001$)

Conscientiousness

A one-way ANOVA, revealed that the three groups differed significantly on conscientiousness ($F = 3.281$, $df = 2,65$, $p = 0.044$).

Table 3.63b: Conscientiousness scores for sub-groups

GROUP	Mean	N	Std. Deviation
CFS	30.562	16	9.0772
DEPRESSED	25.030	33	9.6063
CFS + DEPRESSED	30.267	19	6.1225

However pairwise comparisons (post-hoc Tukey-test) did not find significant differences. There would appear to be a significant trend towards greater conscientiousness in the two CFS groups (with and without depression), which is not detected in the post-hoc test (see Table 3.63b)

When these groups were compared with age as a covariate, conscientiousness scores were not found to differ significantly with age ($F = 2.05$, $df = 1,63$, $p = 0.157$). However the group differences were no longer found to be significant ($F = 1.47$, $df = 2,63$, $p = 0.237$).

As found previously for main group comparisons, age effects appear to have contributed largely to the group differences in conscientiousness.

Openness

A one-way ANOVA, revealed that the three groups differed significantly on openness ($F = 5.164$, $df = 2,65$, $p = 0.002$).

Table 3.63c: Openness scores for sub-groups

GROUP	Mean	N	Std. Dev
CFS	29.840	16	4.8435
DEPRESSED	32.809	33	5.6923
CFS + DEPRESSED	27.569	19	6.5857

Pairwise comparisons confirmed that the depressed group scored significantly higher on openness than the CFS with depression group. The sub groups of CFS were not differentiated on the basis of openness (see table3.63c)

When these groups were compared with age as a covariate, openness was found to differ significantly with age ($F = 11.394$, $df = 1,63$, $p < 0.001$) but not group ($F = 1.65$, $df = 2,63$, $p = 0.2$). The group differences on openness were therefore largely due to age effects.

Agreeableness

A one-way ANOVA, revealed that agreeableness scores did not differ significantly across the groups ($F = 2.99$, $df = 2, 65$, $p = 0.057$) See Table 3.63d.

Table 3.63d: Agreeableness scores for sub-groups

GROUP	Mean	N	Std. Dev
CFS	34.762	16	5.8375
DEPRESSED	29.951	33	6.4973
CFS + DEPRESSED	32.344	19	7.2686

When the groups were compared with age as a covariate, age effects were not significant ($F = 0.57$, $df = 1.63$, $p = 0.45$), as were group effects ($F = 1.99$, $df = 2,63$, $p = 0.145$).

Extraversion

A one-way ANOVA revealed that the three groups differed significantly on extraversion ($F=3.08$, $df =2,65$, $p=0.053$). Pairwise comparisons confirmed that the CFS/only group scores significantly higher on extraversion than the CFS/ with depression group (see Table3.63e)

Table 3.63e: Extraversion scores for sub-groups

GROUP	Mean	N	Std. Dev
CFS	24.28	16	6.0528
DEPRESSED	20.21	33	7.0078
CFS + DEPRESSED	19.09	19	5.9026

When the groups were compared with age at a covariate, age effects were not significant ($F = 0.022$, $df = 1.63$, $p = 0.88$) but the group effects approached significance ($F = 2.97$, $df = 2,63$, $p = 0.06$)

Pairwise comparisons found a significant group effect with the CFS, no depression group scoring significantly higher than the other two groups on extraversion.

(CFS vs. CFS with depression $p = 0.023$)

Depressed vs. CFS with depression $p = 0.55$

CFS vs. CFS/depressed and depressed $p = 0.02$)

3.6.4 Comparison with Test Norms

A significance level $P < 0.01$ was used to control for multiple comparisons using Bonferroni corrections.

Table 3.64 Means and standard deviations for the NEO-FFI scale norms and study groups (Adapted from Costa & McCrae 1992)

		Neuroticism	Extraversion	Openness	Agreeableness	Conscientiousness
Norms (N=968)	mean	19.07	27.69	27.03	32.84	34.57
	S D	7.68	5.85	5.84	4.97	5.88
CFS (N=35)	mean	29.68	21.46	28.61	33.44	30.40
	S D	9.13	6.44	5.88	6.67	7.45
CFS/dep (N=19)	mean	33.2	20.85	27.57	32.34	30.27
	S D	8.17	6.70	6.59	7.27	6.12
CFS/only (N=16)	mean	25.5	24.28	29.84	34.76	30.56
	S D	8.63	6.05	4.84	5.83	9.08
Depressed (N=33)	mean	37.97	20.21	32.81	29.95	25.03
	S D	6.64	7.01	5.69	6.49	9.61

Neuroticism

All groups including sub groups of CFS scored significantly higher on N than test norms; Depression ($p<0.001$), CFS ($p<0.001$), CFS/only ($p=0.009$), CFS and Depression ($p<0.001$).

Extroversion

All groups except CFS/only ($p=0.04$) scored significantly lower on E than test norms; Depression ($p<0.001$), CFS ($p<0.001$), CFS/Depression ($p<0.001$).

Openness

The depressed group scored significantly higher on openness than test norms ($p<0.001$). The CFS main group and sub groups did not differ significantly from test norms on openness; CFS ($p=0.122$), CFS Only ($p=0.03$), CFS/Depression ($p=0.73$).

Agreeableness

None of the groups differed significantly from test norms on agreeableness.

Conscientiousness

All groups, except CFS/only ($p=0.09$), scored significantly lower on C than test norms; Depression ($p<0.001$), CFS ($p=0.002$), CFS/Depression group ($p=0.007$).

3.7 DIMENSIONS OF FAMILY FUNCTIONING

3.7.1 Exploratory data analysis

For all the groups considered in this study, the distributions for all dimensions of family functioning approximated to the normal distribution and there were no problems with kurtosis or skew.

3.7.2 Comparisons across the two main groups: CFS and Depression

None of the ten dimensions of family functioning differed significantly across the two groups(see table 3.72):

Cohesion $t = 1.35, df = 66, p = 0.182$

Expressiveness $t = 0.47, df = 66, p = 0.63$

Conflict $t = 1.52, df = 66, p = 0.134$

Independence $t = 0.40, df = 66, p = 0.69$

Intellectual-cultural $t = 0.31, df = 66, p = 0.76$

Active-recreational $t = 1.28, df = 66, p = 0.21$

Moral-religious $t = 1.69, df = 66, p = 0.1$

Organisation $t = 1.85, df = 66, p = 0.07$

Control $t = 0.40, df = 66, p = 0.69$

Achievement $t = 0.9, df = 66, p = 0.37$

Table 3.72: Dimensions of family functioning for main groups

		Cohesion	Expressiveness	Conflict	Independence	Intelligence
DEPRESSED	Mean	4.587	3.1515	4.6023	5.5758	5.5455
	N	33	33	33	33	33
	Std. Dev.	3.071	2.3200	2.4866	1.7859	2.6112
CFS	Mean	5.600	3.4250	3.6357	5.4036	5.3429
	N	35	35	35	35	35
	Std. Dev.	3.117	2.4461	2.7516	1.7490	2.8174
Total	Mean	5.108	3.2923	4.1048	5.4871	5.4412
	N	68	68	68	68	68
	Std. Dev	3.113	2.3720	2.6518	1.7559	2.7009

		Active-recreation	Moral-religious	Organisation	Control	Achievement
DEPRESSED	Mean	4.4545	3.8485	4.7273	5.7500	5.0606
	N	33	33	33	33	33
	Std. Dev.	2.8733	2.5015	2.8314	1.9804	1.9193
CFS	Mean	5.3143	4.8000	5.8857	5.9429	4.6286
	N	35	35	35	35	35
	Std. Dev.	2.6654	2.1451	2.3361	2.0284	2.0304
Total	Mean	4.8971	4.3382	5.3235	5.8493	4.8382
	N	68	68	68	68	68
	Std. Dev.	2.7813	2.3565	2.6341	1.9926	1.9745

3.7.3 Comparisons across sub-groups: CFS/no depression, CFS/depression and depression

A one-way ANOVA revealed significant differences between the three groups on: Active-recreational ($F = 3.161$, $df = 2,65$, $p = 0.049$) and control dimensions ($F = 3.15$, $df = 2,65$, $p = 0.05$). See table 3..73.

There were no significant differences between the three groups on the remaining eight dimensions of family functioning:

Cohesion $F=1.89$, $df = 2,65$, $p= 0.16$

Expressiveness	$F = 0.21, df = 2, 65, p = 0.81$
Conflict	$F = 1.17, df = 2, 65, p = 0.32$
Independence	$F = 0.24, df = 2, 65, p = 0.79$
Organisation	$F = 2.82, df = 2, 65, p = 0.07$
Achievement	$F = 1.65, df = 2, 65, p = 0.2$
Intellectual-cultural	$F = 1.09, df = 2, 65, p = 0.43$
Moral- religious	$F = 1.44, df = 2, 65, p = 0.24$

Table 3.73: Dimensions of family functioning for sub-groups

		Cohesion	Expressiveness	Conflict	Independence	Intelligence
CFS	Mean	4.8125	3.6250	3.5000	5.5859	4.6250
	N	16	16	16	16	16
	Std. Dev	3.3510	2.8255	3.0551	1.5524	3.1807
DEPRESSED	Mean	4.5871	3.1515	4.6023	5.5758	5.5455
	N	33	33	33	33	33
	Std. Dev	3.0712	2.3200	2.4866	1.7859	2.6112
CFS + DEPRESSED	Mean	6.2632	3.2566	3.7500	5.2500	5.9474
	N	19	19	19	19	19
	Std. Dev	2.8253	2.1411	2.5481	1.9275	2.3915
Total	Mean	5.1085	3.2923	4.1048	5.4871	5.4412
	N	68	68	68	68	68
	Std. Dev	3.1139	2.3720	2.6518	1.7559	2.7009

		Active recreation	Moral-religious	Organisation	Control	Achievement
CFS	Mean	4.2500	4.6875	5.1875	5.0625	4.0625
	N	16	16	16	16	16
	Std. Dev	2.6708	2.1952	2.7621	2.2351	1.9483
DEPRESSED	Mean	4.4545	3.8485	4.7273	5.7500	5.0606
	N	33	33	33	33	33
	Std. Dev	2.8733	2.5015	2.8314	1.9804	1.9193
CFS + DEPRESSED	Mean	6.2105	4.8947	6.4737	6.6842	5.1053
	N	19	19	19	19	19
	Std. Dev	2.3706	2.1575	1.7754	1.5294	2.0247
Total	Mean	4.8971	4.3382	5.3235	5.8493	4.8382
	N	68	68	68	68	68
	Std. Dev	2.7813	2.3565	2.6341	1.9926	1.9745

When this analysis was repeated with Age as covariate, the results were as follows:-

Active-recreational dimension

Age effects were not found to be significant ($F = 0.107$, $df = 1, 63$, $p = 0.74$), and the group effect persisted at the same level of significance ($F = 3.117$, $df = 2, 63$, $p < 0.05$).

Pairwise comparisons confirmed that there was a significant group effect with the CFS/depression group scoring significantly higher on this dimension than the other two groups

(CFS vs. CFS/depression	$p = 0.0376$
Depressed vs. CFS/depression	$p = 0.032$)

Control dimension

Age effects were found to be significant ($F = 4.97$, $df = 1,63$, $p = 0.03$), but the group effect persisted at the same level of significance ($F = 3.23$, $df = 2,63$, $p = 0.046$). Pair-wise comparisons , confirmed a significant group effect with the CFS/no depression group scoring significantly less on the control dimensions than the other two groups.

(CFS vs. CFS/depression	$p = 0.016$
Depression vs. CFS/depression	$p = 0.47$
CFS vs. CFS/depression + depression	$p = 0.016$)

Organisation dimension

This dimension of Family Functioning was found to be significantly affected by age ($F = 11.919$, $df = 1,63$, $p = 0.001$), but not group ($F = 1.12$, $df = 2,63$, $p = 0.333$).

For the remaining seven dimensions, age and group effects were found to be non-significant.

3.7.4 Comparisons with Test Norms

A significance level $P < 0.01$ was used to control for multiple comparisons using Bonferroni corrections.

Table 3.74: Subscale means and standard deviations for FES norms, and study groups (Adapted from Moos and Moos, 1987)

		Cohesion	Expressiveness	Conflict	Independence	Achievement	Intelligence	Active-recreation	Moral-religious	Organisation	Control
Norms (N=1125)	Mean	6.61	5.45	3.31	6.61	5.47	5.63	5.35	4.72	5.41	4.34
	SD	1.36	1.55	1.85	1.19	1.62	1.72	1.87	1.98	1.03	1.81
CFS (N=35)	Mean	5.6	3.43	3.64	5.40	4.62	5.34	5.31	4.8	5.89	5.94
	SD	3.12	2.45	2.75	1.75	2.03	2.83	2.66	2.14	2.34	2.03
Depressed (N=33)	Mean	4.59	3.15	4.60	5.58	5.06	5.55	4.45	3.85	4.72	5.75
	SD	3.07	2.32	2.49	1.79	1.92	2.61	2.87	2.50	2.83	1.98
CFS/dep (N=19)	Mean	6.26	3.26	3.75	5.25	5.11	5.95	6.21	4.89	6.47	6.68
	SD	2.83	2.14	2.55	1.93	2.02	2.39	2.37	2.16	1.78	1.52
CFS/only (N=16)	Mean	4.81	3.63	3.50	5.59	4.06	4.62	4.35	4.69	5.19	5.06
	SD	3.35	2.83	3.06	1.55	1.95	3.18	2.67	2.19	2.76	2.24

Cohesion

The depressed group scored significantly lower on cohesion ($p < 0.001$). The main CFS group and subgroups did not differ significantly from test norms; CFS ($p = 0.06$), CFS/only ($p = 0.05$), CFS/Depression ($p = 0.59$).

Expressiveness

All groups except CFS/only ($p=0.02$) scored significantly lower only expressiveness than test norms; Depression ($p<0.001$), CFS ($p<0.001$), CFS/Depression ($p<0.001$).

Conflict

The depressed group scored significantly higher on conflict than test norms ($p=0.005$). The CFS group and subgroups did not differ significantly from test norms.

Independence

All groups except CFS/only ($p=0.02$) scored significantly lower than test norms on independence; Depression ($p=0.002$), CFS ($p<0.001$) CFS/Depression ($p<0.007$).

Achievement Orientation

The CFS/only subgroup scored significantly less than Test Norms on achievement orientation ($p=0.01$). All other groups did not differ significantly from Test Norms on achievement orientation; Depression ($p=0.23$), CFS ($p=0.02$), CFS/only ($p=0.44$).

Intellectual-Cultural Orientation

None of the groups or subgroups differed significantly from test norms on this dimension.

Active-Recreational Orientation

None of the groups or subgroups differed significantly from test norms on this dimension.

Moral Religious Orientation

None of the groups differed significantly from test norms on this dimension.

Organisation

None of the groups differed significantly from test norms on this dimension.

Control

All groups except, CFS/only ($P=0.22$) scored significantly higher on this dimension than test norms; Depression ($P<0.001$), CFS ($P<0.001$), CFS/Depression ($P<0.001$).

4 DISCUSSION

4.1 MAIN FINDINGS

4.1.1 Psychiatric Comorbidity

The study lends further support to the substantial body of previous research, which has found high levels of psychiatric comorbidity accompanying CFS. Seventy-one per cent of the CFS group were categorised as suffering from a psychiatric disorder during the course of their illness. This prevalence figure lies at the upper end of the range for prevalence (50-75%) reported in previous studies (Lane et al 1991; Kruesi et al 1989) and it is possible that reliance upon casenote information as a method of identifying psychiatric disorder in the CFS sample may have increased the estimated prevalence slightly. Fifty-four per cent of the CFS sample were categorised on the basis of clinician diagnosis as suffering from concurrent depressive disorder during the course of their illness. Again this figure is comparable to prevalence figures reported in previous studies (Wessely and Powell 1989 – 47%; Kruesi et al 1989 – 46%; Hickie et al 1990 – 45.8%). A further 40% of the CFS group satisfied HADS criteria for current depressive disorder. The lower figure for affective disorder using HADS criteria may reflect the reduction of depressive symptoms due to antidepressant medication or possibly the limited effectiveness of the HADS as a case finding tool for CFS patients.

Consistent with previous research (Wessely and Powell 1989; Wood et al 1991) the prevalence of concurrent anxiety disorder (37%) was less than the prevalence figure for depression. Seven out of the thirteen cases of clinical anxiety

were also diagnosed as having a depressive disorder and it may therefore be argued that clinical anxiety was secondary to depressive disorder in these cases. The high proportion of the CFS group satisfying HADS criteria for caseness, both depression and anxiety, further supports this assumption. The percentage of CFS patients satisfying HADS criteria for anxiety is probably the best indicator for anxiety disorder in this group and at 25% is comparable with previous research which found a higher point prevalence for anxiety disorders than in community samples (Kruesi et al, 1989; Wood et al, 1991). As with major depressive disorder, a number of anxiety symptoms potentially overlap with CFS and several alternative hypotheses have been advanced to explain these findings. Increased anxiety may be viewed as an understandable reaction to debilitating illness and a number of pathophysiological mechanisms may be involved in the production of anxiety symptoms in medically ill patients (Derogatis and Wise, 1989).

The percentage of CFS patients in this study found to have prior psychiatric history (42%) is comparable to that found by Wessely and Powell (1989 – 43%) and significantly higher than the lifetime prevalence rates for psychiatric disorders reported in three large scale community epidemiological surveys (23.9-26.2%) (Robins, Helzer, & Weissman, 1984). The estimated prevalence of premorbid affective disorder (31.4%) was lower than has been found previously (Taerk et al, 1987 – 50%; Gold et al, 1990 – 50%; Katon et al, 1991 – 53%) but higher than that found by Hickie et al (1990 – 12.5%). The study's findings would appear to suggest that a substantial proportion of the CFS group with concurrent depressive disorder were not depressed prior to the onset of their illness. The depression vulnerability hypothesis, which proposes that premorbidly depressed people are susceptible to the

development of depression and fatigue following viral illness, would not seem to be supported for these individuals. The current estimate however must be interpreted cautiously as it was made on the basis of case note information and it is therefore possible that some cases of premorbid effective disorder were not detected if such information is not recorded in the casenotes.

4.1.2 Psychological distress

As predicted the subgroups of CFS with and without concurrent depression were found to be differentiated on emotional distress as measured by HADS total scores. The existence of a clear subgroup of CFS without concurrent depression and demonstrating significantly less psychological distress argues against psychiatric theories as a total explanation for CFS. This finding fits with previous studies, which have consistently found a significant subgroup of CFS (between one and two thirds of cases), without depressive/psychiatric disorders (Hickie et al, 1990; Taerk et al, 1989; Manu et al, 1988; Kruesi et al, 1989). Although the subgroups of CFS, with and without depression, were not differentiated on the basis of symptom severity (HADS depression and anxiety subscale scores) or caseness, for all these measures, it was found that the depressed CFS group more closely resembled the depressed group than the non-depressed CFS group. This finding contrasts to that of Powell et al (1990), who found significant differences in symptom severity using the HADS depression subscale between a depressed CFS group and a depressed group. However the depressed group in Powell et al's study was drawn from a psychiatric inpatient population and may therefore have been less comparable with a depressed CFS group than was the case in this study.

Overall the findings of the current study support the view of CFS as a heterogeneous disorder, comprising of subgroups differentiated in terms of psychological distress and psychiatric morbidity.

4.1.3 Fatigue

An important finding of this study was that the CFS group and depressed group did not differ significantly in terms of self-reported fatigue and this remained the case when the CFS group was further divided into subgroups, with and without depression. This finding fits with previous research, which found no significant differences between a group of CFS patients, and depressed patients on measures of either physical or mental fatigue (Wessely and Powell, 1989). It cannot be assumed on the basis of these similarities that CFS is an atypical manifestation of depression, although fatigue in both disorders may have the same biological mechanisms as suggested by Wessely and Powell (1989).

Consistent with previous research (Lawrie and Pelosi, 1995; Pawlikowska et al, 1994) a significant correlation was found between fatigue states and emotional distress for the data set as a whole ($p < 0.01$). Interestingly, however, this correlation was found to be highly significant for the depressed group ($p = 0.002$) and only approached significant for the subgroups of chronic fatigue syndrome ($p = 0.07$). This finding would appear to suggest that a stronger relationship exists between emotional distress and fatigue in the depressed group compared with depressed and non-depressed CFS groups. The findings for the CFS groups are similar to those of previous studies, which have examined the relationship between fatigue severity and depressive symptoms in multiple sclerosis and systemic lupus (Krupp, Alvarez, &

LaRocca, 1988; Krupp, LaRocca & Nash, 1990). Low non-significant correlations were reported for these groups and the CFS patients in this study would appear to more closely resemble these patients than those suffering from major depressive disorder. Again these findings lend to support the view of CFS as distinct and different from depression with fatigue.

The pattern of fatigue attribution in the depressed group was very distinct with the majority (70%) giving a primary psychological reason and only 1 out of 32 giving a primary physical reason. In contrast the proportion of subjects in the CFS group giving a primary psychological or physical reason for their fatigue was lower (14% and 34% respectively). The majority of the CFS group (48%) gave other responses including: mixed reasons, don't know, or no response. This pattern of fatigue attribution in the CFS group contrasts with that found by Powell et al (1990) where 80% of the CFS patients attributed their illness to a physical cause. The significantly smaller number of patients in this study giving a physical attribution for their fatigue may possibly be explained by the educative element of their treatment, which encouraged a multifactorial conceptualisation of CFS. Alternatively, it may be explained by the fact that subjects in this study were asked to give presumed reasons for their fatigue, rather than reasons for their illness, as in Powell et al's study. As has been found previously (Wessely and Powell, 1989; Powell et al, 1990) the study found that primary psychological attribution for fatigue was significantly greater in the depressed group ($p < 0.001$) and primary physical attribution was significantly greater in the CFS group ($p < 0.001$). These findings however appear to reflect the very strong bias towards psychological attribution in the depressed group, the bias towards physical attribution in the CFS group being much less extreme. As was

found by Powell et al (1990), when the subgroups were compared, the depressed CFS group was found to demonstrate a significantly greater primary physical attribution and significantly lower primary psychological attribution than the depressed group. In Powell et al's study it was suggested that the difference in attribution between these groups may be suggestive of an outward style of attribution protecting the self esteem of depressed CFS patients but at the expense of greater vulnerability to somatic symptoms. It seems equally possible that the attribution of fatigue in these groups reflect what the patient considers to be their primary diagnosis: depression or CFS, and is influenced by the type of treatment received: psychiatric or medical. As mentioned later, another drawback of the current study is that subjects were asked to give what they considered were "the reasons for their fatigue" rather than more specifically "the reasons for their illness. It is possible that the reasons given by subjects for their fatigue symptoms may have differed from the reasons they would have given for their illness more generally and this was probably a source of inaccuracy in the current study. In retrospect, a more precise question or one giving a list of possible reasons for their symptoms would have allowed a more scientific examination of the question of attribution.

4.1.4 Personality factors

Neuroticism

Consistent with other studies that have found elevated levels of personality pathology in CFS patients compared with controls (Millon et al, 1989; Blakely et al, 1991), the current study found significantly more trait neuroticism in the main CFS group compared with test norms ($p < 0.001$). Consistent with Johnson et al's (1996) findings, the CFS group was also found to demonstrate significantly less trait

neuroticism than the depressed group ($p=0.016$). It was further shown that the depressed CFS patients more closely resembled the depressed patients in terms of neuroticism than the non-depressed CFS patients. However in contrast to Johnson et al (1996) who found the non-depressed CFS patients didn't differ significantly from healthy controls in terms of neuroticism, the non-depressed CFS patients in this study were found to score significantly higher on N than test norms ($p=0.009$). As discussed later, comparison with test norms in the current study are flawed for a number of reasons and Johnson et al's findings, being based on comparison with a matched control group, are very probably more reliable in this respect than those of this study.

This study's finding of two distinct groups of CFS, distinguishable on the basis of concurrent depressive disorder, psychological distress and associated trait neuroticism supports the view of CFS as a heterogeneous disorder. The studies findings do not support the view of CFS (in non-depressed patients) as a form of "masked depression" with predominantly somatic symptoms. With respect to the relationship between neuroticism, depressive disorder and chronic fatigue syndrome several possibilities exist. Firstly, the possibility of CFS as a manifestation of depressive disorder whereby neurotic individuals are more likely to become depressed in aversive situations (under stress) and resulting affective states may then lead to increased reporting of physical symptoms (Gray, 1981). Another possibility is that individuals with high neuroticism are vulnerable to depression, which serves as a vulnerability factor for the development of CFS (depression vulnerability hypothesis) or alternatively individuals with high N are more likely to develop depression in response to CFS (reactivity hypothesis). Finally, it is possible that

diagnosis of concurrent depression in CFS is somewhat of a red herring and in fact CFS and depression are different disorders with overlapping symptoms, a view supported by studies which have found differences between CFS patients and depressed patients in respect of 5-HT neurotransmission (Bakheit et al; 1992, Cleare et al; 1995 and Sharpe et al; 1996) and the neuroendocrine hormone cortisol (Demitrack, 1987; Cleare et al, 1995). If this view is accepted, it is possible that increased neuroticism may be associated with vulnerability to developing chronic fatigue syndrome in response to stress. The study's finding of similarity between depressed CFS patients and depressed patients in terms of high neuroticism would appear to provide evidence against the "organic hypothesis" as an explanation for depression in these CFS patients.

Conscientiousness

The least expected results of this study were those relating to conscientiousness, where, contrary to predictions, the CFS group and subgroups were not found to differ significantly from the depressed group and all groups, with the exception of non-depressed CFS patients, scored significantly lower on conscientiousness than test norms. It had been predicted that the CFS group and subgroups would score significantly higher than both the depressed group and test norms on conscientiousness. These findings are consistent with those of Wood and Wessely (1999) who found no differences between chronic fatigue syndrome patients and rheumatoid arthritis patients on measures of perfectionism and social desirability. They may therefore be interpreted as providing further evidence against the view of CFS patients as being achievement oriented perfectionist individuals, proposed by the cognitive behavioural model of chronic fatigue syndrome. These results must

however be interpreted with caution as a number of the methodological limitations discussed later, including the problem of comparing small groups with test norms and small sub sample sizes may have contributed to the study's non significant findings. The NEO-FFI norms for conscientiousness are also considered by some personality theorists to be higher than would be expected (Ian Deary, personal communication), and comparison with a matched control group would therefore have been of particular value when examining conscientiousness. However such methodological limitations would not appear to account for the finding of non-significant differences between the main groups of depressed and chronic fatigue syndrome patients.

It is also possible that the responses of the CFS patients to items measuring conscientiousness on the NEO-FFI were affected by their symptomatology and/or adjustments made to thinking and behaviour as a consequence of their illness. For example in relation to the following items:

"I work hard to accomplish my goals"

"I am a productive person and always get the job done"

"I have a clear set of goals and work towards them in a methodological fashion"

It seems likely that CFS patients will have been forced to change the way they might previously have responded to such items in order to adapt to the debilitation associated with CFS. Similarly it is likely that many CFS patients through their treatment will have been encouraged to change beliefs and behaviours linked with high conscientiousness, which are considered within the cognitive model to be maintaining factors for chronic fatigue. It is therefore proposed that current conscientiousness scores on the NEO- FFI are likely to be significantly lower than

pre-morbid scores for CFS patients. The NEO- FFI was therefore probably a poor measure of pre-morbid conscientiousness for this group.

Extraversion

All groups except the non-depressed CFS groups scored significantly lower than test norms on extraversion and the non-depressed CFS group scored significantly higher than the depressed CFS group and the depressed group. An association between high neuroticism, low extraversion and low affect has been extensively reported in the literature (Watson & Clark, 1992) so the pattern of low extraversion corresponding with high neuroticism found for the depressed groups was predictable. As mentioned later, responses to a number of items on the extraversion scale of the NEO FF-I are likely to have been adversely affected by fatigue symptoms. As a result of this flaw, it is likely that the extraversion scores for the CFS group are underestimated and this should be considered when interpreting these results.

Openness and agreeableness

No significant differences were found between the comparison groups in terms of agreeableness. The depressed group were found to have scored significantly higher than test norms on openness, which is probably a reflection of the sampling bias in the depressed group or possibly age effects. Openness scores have been found to be modestly associated with both education and measured intelligence (Costa & McCrae, 1992) which would be expected to be high in a sample consisting largely of university undergraduates.

4.1.5 Family functioning

Firstly, in relation to the fifth hypothesis, this study did not find evidence of family belief systems, which might be implicated in the development of those predisposing personality features proposed within the cognitive behavioural model of CFS. Contrary to predictions, the main CFS group and depressed CFS subgroup were not found to differ significantly from the depressed group or test norms on achievement orientation. The non-depressed CFS group was found to score significantly lower than test norms on achievement-orientation, which was a difference in the opposite direction to that predicted. Similarly, contrary to predictions, none of the groups were found to differ significantly from test norms on active-recreational orientation and the depressed CFS group was found to score significantly higher on this dimension than the non-depressed CFS group. One possible explanation for this unexpected finding is that reduced activity and loss of recreational interests resulting from CFS may be experienced more negatively by those patients coming from a family background where active recreational pursuits were encouraged, so increasing vulnerability to a reactive depression. While this study did not find evidence of family functioning which might be presumed to influence the development of those predisposing personality factors for CFS proposed by the cognitive behavioural model, it may be that such personality features are largely genetically determined. The methodological limitations discussed later, particularly those relating to small sample sizes and the use of American norms based on large sample sizes, may also have contributed to the study's findings, which must therefore be interpreted with caution.

Secondly, in relation to the fourth hypothesis, the study produced mixed findings in respect of predictions made relating to somatisation as a theory relevant to CFS. Consistent with predictions, no differences were found between the groups on those dimensions of family functioning, which had been associated with somatising families (Minuchin, 1975; Garralda, 1992). However contrary to predictions, all groups, except the non-depressed CFS group, were found to score lower than test norms on emotional expressiveness. A pattern of low emotional expressiveness in families has been linked to the development of alexithymia (Lipowski, 1990), which is implicated in some theories of somatisation. However, alexithymia has also been found to be associated with depression in the general population (Honkalamps et al, 2000), which would seem to suggest that depressed patients also tend to somatise distress. The findings of the current study suggest that a pattern of low emotional expressiveness in families may be an aetiological factor in both depression and CFS with concurrent depression. However, the limitations of this study, particularly the use of American norms and the massive differences in the size of study samples and norm samples mean that the findings in respect of emotional expressiveness are possibly unreliable and would need to be replicated through further research.

Finally, in relation to other dimensions of family functioning, the non-depressed CFS group was found to score lower on the control dimension than both the depressed CFS group and the depressed group. Compared to test norms the non-depressed CFS group was found to differ the least, exhibiting only lower achievement orientation. The depressed CFS group exhibited more dysfunction, scoring lower on independence and expressiveness and higher on control. The

families of depressed patients appeared to demonstrate most dysfunction relative to norms, exhibiting lower independence, cohesion and expressiveness and higher conflict and control. These findings suggest that family dysfunction plays a greater part in the aetiology of depression than CFS, and again supports the existence of sub-groups of CFS with different aetiological factors.

4.2 METHODOLOGICAL LIMITATIONS

The current study can be criticised on the grounds of a selection bias applicable to both CFS and depressed samples. The CFS group was drawn from a hospital population, either an Infectious Diseases Unit (N=28) or Psychiatric/Clinical Psychology Outpatient Services. Several studies have found evidence that the demographic and psychiatric associations of CFS are different in community samples compared with hospital populations (Lloyd et al 1990; Buchwald, 1995; Lawrie and Pelosi, 1995; and Euba et al, 1990). Patients in the CFS group were therefore probably not representative of CFS sufferers seen in Primary Care.

Similarly, the depressed group also reflected a degree of selection bias, most of the sample (24/33) having been drawn from a university psychiatric service. A significant proportion of these patients suffered from severe and long-standing depression with an early onset, likely to be indicative of “endogenous” depressive illness with a largely biological causation. Again these patients were therefore not representative of depressed patients seen in Primary Care.

This kind of selection bias is a feature of a great many previous studies relating to CFS (Taerk et al, 1987; Hickie et al, 1990) and must be taken into account

when interpreting results. The findings of the current study can therefore not be generalised to those CFS patients seen outside the specialist setting. One advantage of drawing subjects from a hospital population was that there was probably greater certainty regarding clinical diagnoses, particularly in the case of CFS, than there might otherwise have been in a primary care population.

In addition to the selection bias arising from recruitment of subjects from a hospital population, the low response rate for those CFS patients approached by post, suggests that they were not representative of patients attending the infectious diseases unit. It is therefore likely that a further selection bias was applicable to this subgroup of the CFS sample. In contrast, the good response rate for depressed patients attending the university psychiatric service, suggests that this subgroup of the depressed sample were representative of patients seen in this clinical setting. Unfortunately, the response rates for patients recruited to both samples by other clinicians were not recorded so it was not possible to determine the response rates for the complete samples. Similarly, demographic information for patients who did not return questionnaires was not accessible, so it is not possible to comment further on the kinds of biases that may have been introduced to the CFS sample due to the low response rate.

A significant drawback of the current study is the absence of a normal control group of healthy subjects, which would have allowed for a more meaningful interpretation of results. Test norms for the NEO-FFI and FES were available for comparison but such comparisons are flawed for a number of reasons. Firstly, test norms relate to very large sample sizes (FES, N=1125, NEO-FFI, N=983) and the

sample sizes in the current study are extremely small by comparison. Secondly test norms are based upon an American population and therefore not representative of the Scottish population from which the samples in the current study were drawn. The findings of comparisons with tests norms in this study therefore need to be interpreted with caution and would need to be replicated through further research.

The small size of the CFS subgroups (N=16, N=19) is another significant limitation of the current study. Although the size of the main comparison groups: CFS and depression were adequate (N=35, N=33) there is insufficient power in the study to detect significant differences between the subgroups, based upon a power calculation (Cohen, 1992). Assuming a medium effect size, the power achieved in this study for subgroup comparisons was 0.68 and an additional nine subjects (N=25) would have been needed to achieve sufficient power (Clark-Carter, 1997). The study's findings in respect to subgroup comparisons therefore need to be interpreted with caution.

This study bears witness to the difficulty of diagnosing depressive disorder in patients with CFS, due to the significant degree of symptom overlap (Rae, 1991). In this study, practical limitations meant that the categorization of depression in CFS patients during the course of their illness was made on the basis of clinician diagnosis (Consultant Physician for those patients attending the infectious diseases unit) sometimes but not always accompanied by a diagnosis from psychiatry. As a further check case notes were also examined against a checklist of depressive symptomatology (DSM-IV). This methodology is clearly less precise and more subjective than diagnosis using a diagnostic instrument such as the structured clinical

interview for DSM III-R (Hickie et al, 1990) or the diagnostic interview schedule (Taerk et al, 1987). Unlike these studies the current study aimed to identify patients who had suffered depression during the course of their illness, many of whom were substantially improved following treatment, making use of such a diagnostic instrument inappropriate. However it remains the case that reliance upon clinician diagnosis may have reduced the reliability of depressive diagnosis in the CFS group and this shortcoming should be considered when interpreting the results of this study.

Another limitation of the study was that both samples: CFS and depressed, consisted of patients “in treatment”, many of whom were in receipt of antidepressant medication. Unfortunately, use of antidepressants was not recorded as a variable and therefore not entered into subsequent data analyses. It is therefore possible that antidepressant medication acted as a confounding factor for other measures: fatigue and emotional distress, in this study. However it is hoped that as the majority of depressed patients in both groups were treated with antidepressants any such effects would balance out between the groups.

Finally a number of criticisms can be made in respect of the measures employed in the current study. Firstly, although many studies support the use of the HADS depression subscale as a screening instrument in a hospital population (Lewis and Wessely, 1990; Aylard et al, 1987), it is considered that exclusion of all symptoms other than anhedonia on this scale is likely to make it a limited measure of symptom severity for this group. In contrast, the anxiety sub scale of the HADS appears more inclusive of a range of anxiety symptoms and therefore possibly a more valid measure of symptom severity. The proposed shortcomings of the HADS reflect

the significant problem of diagnosis of depression in CFS, which has been widely discussed in the literature (Rae, 1991; David, 1991). In retrospect it would have been interesting to compare the HADS with other measures of depression in this study, possibly the Beck Depression Inventory (Beck, 1978) scoring cognitive-effective and systemic items separately (Cavanaugh, Clark & Gibbons, 1983) or the profile of mood states (McNair, Lorr & Droppleman, 1971) as was used by Millon et al (1989).

One item on the HADS depression subscale “I feel as if I am slowed down” was consistently scored highly by the CFS group and would seem to have been influenced by fatigue state. However criteria for caseness, depression, using the HADS, was not changed to adapt for this probable flaw, in view of the presumed underestimation of symptom severity due to the scales primary focus upon anhedonic state.

Similarly a number of items on the extraversion subscale of the NEO- FFI are likely to have been significantly affected by CFS symptomatology. Examples include item 32 “I often feel as if I am bursting with energy”, and item 22 “I like to be where the action is”. Such contamination almost certainly limits this sub scale as a measure of extraversion in this group. Fortunately this personality domain was the not the focus of the research hypotheses, although it is possible that the conscientiousness subscale, which was central in this study, may also be subject to similar problems. These problems and their implications for results are discussed later in this section.

Finally, with respect to the FES, subjects were asked to complete this questionnaire retrospectively and responses may therefore have been confounded by memory bias. However it could be argued that the lasting impressions of family life are more important and valid than childhood impressions.

4.3 CONCLUSIONS

This study bears witness to the high degree of psychiatric comorbidity in CFS.

The study's findings support the view of CFS as a heterogeneous disorder with at least two distinct subgroups distinguishable on the basis of psychological distress/depressive disorder and associated trait neuroticism. A case is made for multiple aetiologies in relation to CFS with multiple factors contributing to the syndrome in different subgroups.

This study found no evidence of the predisposing personality factors: for CFS proposed by the cognitive behavioural model.

Overall this study's findings in relation to neuroticism, fatigue, and to some extent, family functioning, do not support the view of CFS, without concurrent depression, as a form of "masked depression". Although similarities were found to exist between depressed CFS patients and patients with major depressive disorder, the study found evidence of less neuroticism and less family dysfunction in the depressed CFS patients. After consideration of the current findings and those of previous research, it is proposed that there are two likely explanations for the relationship between high neuroticism, depressive disorder and CFS, which may apply to sufferers of CFS. Firstly, the reactivity hypothesis, whereby high neuroticism increases the risk of developing a depressive disorder in response to the

debilitation caused by CFS. Alternatively, CFS and depression may represent different syndromes with overlapping symptoms, involving the same underlying biological systems. In accordance with the Goldberg and Huxley's model of psychiatric illness it is considered that both syndromes may be triggered in response to stress and/or illness. High neuroticism is associated with a poor ability to cope with stress and can therefore be considered to be a vulnerability factor for the development of both CFS and depression.

This studies findings fit with those of previous research supporting the view of CFS as a heterogeneous disorder with a number of different aetiologies. It is suggested that future research should focus more upon investigating the differences between different clinical presentations of CFS, in an attempt to unravel the aetiological factors relating to different sub-types of the disorder.

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APPENDIX

Appendix I

THE HOSPITAL ANXIETY AND DEPRESSION SCALE

This questionnaire will help us know how you are. Read each item and underline the response that comes closest to how you have felt in the last few days. Don't take too long over your replies, your immediate reaction will probably be more accurate

Name..... Age..... Sex..... Date.....

A I feel tense or "wound up"

- 3 - most of the time
- 2 - a lot of the time
- 1 - from time to time, occasionally
- 0 - not at all

D I feel as if I am slowed down

- 3 -nearly all the time
- 2 -very often
- 1 -sometimes
- 0 -not at all

D I still enjoy the things I used to enjoy

- 0 -definitely as much
- 1 -not quite so much
- 2 -only a little
- 3 -hardly at all

A I get a sort of frightened feeling like butterflies in my stomach

- 0 -not at all
- 1 - occasionally
- 2 -quite often
- 3 - very often

A I get a sort of frightened feeling as if something awful is about to happen

- 3 - very definitely and quite badly
- 2 - yes but not too badly
- 1 - a little, but it does not worry me
- 0 - not at all

D I have lost interest in my appearance

- 3 - definitely
- 2 -I dont take as much care as I should
- 1 -I may not take quite as much care
- 0 - I take as much care as ever

D I can laugh and see the funny side of things

- 0 - as much as I always could
- 1 - not quite so much now
- 2 - definitely not so much now
- 3 - not at all

A Worrying thoughts go through my mind

- 3 - a great deal of the time
- 2 - a lot of the time
- 1 - from time to time but not too often
- 0 - only occasionally

D I feel cheerful

- 3 - not at all
- 2 - not often
- 1 - sometimes
- 0 - most of the time

A I can sit and feel relaxed

- 0 - definitely
- 1 - usually
- 2 - not often
- 3 - not at all

A I feel restless as if I have to be on the move

- 3 - very much indeed
- 2 - quite a lot
- 1 - not very much
- 0 - not at all

D I look forward with enjoyment to things

- 0 - as much as I ever did
- 1 - rather less than I used to
- 2 - not very much
- 3 - hardly at all

A I get sudden feelings of panic

- 3 - very often indeed
- 2 - quite often
- 1 - not very often
- 0 - not at all

D I can enjoy a good book, radio or TV programme

- 0 - often
- 1 - sometimes
- 2 - not often
- 3 - very seldom

Appendix II

FATIGUE QUESTIONNAIRE

We would like to know whether or not you have been having any problems with feeling tired, weak or lacking in energy in the last month. Please answer ALL the questions simply by underlining or ticking the answer which you think most clearly applies to you. We also would like to know how you feel either at the moment or recently, rather than a long time ago. If you have been feeling tired for a long time, we want you to compare yourself to how you felt when last well.

Name -----

Date -----

Do you have problems with tiredness ?	less than usual	no more than usual	more than usual	much more than usual
Do you need to rest more?	less than usual	no more than usual	more than usual	much more than usual
Do you feel sleepy or drowsy ?	less than usual	no more than usual	more than usual	much more than usual
Do you have problems starting things ?	less than usual	no more than usual	more than usual	much more than usual
Do you lack energy ?	better than usual	no more than usual	more than usual	much more than usual
Do you have less strength in your muscles ?	better than usual	no more than usual	more than usual	much more than usual
Do you feel weak ?	less than usual	same as usual	more than usual	much more than usual
Do you have difficulty concentrating ?	less than usual	same as usual	more than usual	much more than usual
Do you make slips of the tongue when speaking ?	less than usual	no more than usual	worse than usual	much worse than usual
Do you find it more difficult to find the correct word	less than usual	no more than usual	worse than usual	much worse than usual
How is your memory ?	Better than usual	no worse than	worse than	much

usual

usual

worse than
usual

The next questions ask about muscle pain

Do your muscles hurt at rest ?

less than usual

no worse than
usual

worse than
usual

much
worse than
usual

Do your muscles hurt after
exercise ?

less than usual

no more than
usual

worse than
usual

much
worse than
usual

If you are tired at the moment, please indicate approximately how long this has lasted. (Please circle the answer which applies to you)

less than 1 week

less than 3
months

between
3 and 6
months

6 months
or more

Overall, what percentage of the time do you feel tired
(Please circle the answer which applies to you)

25% of
the time

50% of
the time

75% of
the time

All the
the time

Why do you think you are feeling tired ? please give a reason

Appendix III

FAMILY ENVIRONMENT SCALE

There are 90 statements in this Questionnaire. They are statements about families. You are to decide which of these statements are true of your **family of origin (Your parents and siblings)** and which are false. We want you to complete the questionnaire retrospectively, remembering that the questions apply to the family **family you grew up with rather than your current family (your spouse and children)** .If you think the statement is *true* or mostly *true* of you family of origin, circle the **T** response option. If you think the statement is *false* or mostly *false* of your family of origin, circle the **F** response option.

You may feel that some of the statements are true for some of your family members and false of others, mark T if the statement is *true* for most members. Mark F if the statement is *false* for most members. If the members are equally divided, decide what is the stronger overall impression and answer accordingly.

Remember, we would like to know what your family seems like to *you*. So *do not* try to figure out how other members see your family, but *do* give us your general impression of your family for each statement.

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name ----- age ----- sex----- date -----

Please tick the following response categories to describe the composition of your family of origin (the family you lived with for most of your childhood)

mother

father

stepmother

stepfather

sister /s **how many?**

brother/s **how many?**

half-brother/sister/s **how many?**

Other family member e.g. grandparent state who -----

The following questions are optional, so you do not have to answer them if you would prefer not to.

Did your parents separate or divorce yes / no

If you answered yes to the above question, what was your age at that time ----- yrs

Did you suffer the death of a parent **yes / no**

If you answered yes to the above question, what was your age at that time ----- yrs

Were you bought up mainly by a lone parent **yes / no**

1. Family members really helped and supported one another	T	F
2. Family members often kept their feelings to themselves	T	F
3. We fought alot in our family	T	F
4. We didn't do things on our own very often in our family	T	F
5. We felt it was important to be the best at whatever we did	T	F
6. We often talked about political and social problems	T	F
7. We spent most weekends and evenings at home	T	F
8. Family members attended church (place of Worship) or Sunday school fairly often	T	F
9. Activities in our family were pretty carefully planned	T	F
10. Family members were rarely ordered around	T	F
11. We often seemed to be killing time at home	T	F
12. We said anything we wanted to around home	T	F
13. Family members rarely became openly angry	T	F
14. In our family, we were strongly encouraged to be independent	T	F
15. Getting ahead in life was very important in our family	T	F
16. We rarely went to lectures, plays or concerts	T	F
17. Friends often came over for dinner or to visit	T	F
18. We didn't say prayers in our family	T	F
19. We were generally very neat and orderly	T	F
20. There were very few rules to follow in our family	T	F
21. We put a lot of energy into what we did at home	T	F

22. It was hard to “blow off steam” at home without upsetting somebody	T	F
23. Family members sometimes got so angry they threw things	T	F
24. We thought things out for ourselves in our family	T	F
25. How much money a person makes was not very important in our family	T	F
26. Learning about new and different things was very important in our family	T	F
27. Nobody in our family was active in sports	T	F
28. We often talked about the religious meaning of Christmas or other holidays	T	F
29. It was often hard to find things when you needed them in our household	T	F
30. There was one family member who made most of the decisions	T	F
31. There was a feeling of togetherness in our family	T	F
32. We told each other about our personal problems	T	F
33. Family members hardly ever lost their tempers	T	F
34. We came and went as we wanted to in our family	T	F
35. We believed in competition and “may the best man win”	T	F
36. We were not that interested in cultural activities.	T	F
37. We often went to the cinema, sports events, or for days out e.t.c.	T	F
38. We didn’t believe in heaven or hell.	T	F
39. Being on time was very important in our family.	T	F

40. There were set ways of doing things at home.	T	F
41. We rarely volunteered when something had to be done at home	T	F
42. If we felt like doing something on the spur of the moment we often just did it	T	F
43. Family members often criticised each other.	T	F
44. There was very little privacy in our family.	T	F
45. We always strove to do things just a little bit better the next time.	T	F
46. We rarely had intellectual discussions.	T	F
47. Everyone in our family had a hobby or two.	T	F
48. Family members had strict ideas about what was right or wrong.	T	F
49. People changed their minds often in our family.	T	F
50. There was a strong emphasis on following the rules in our family.	T	F
51. Family members really backed each other up.	T	F
52. Someone usually got upset if you complained in our family.	T	F
53. Family members sometimes hit each other.	T	F
54. Family members almost always relied on themselves when a problem came up	T	F
55. Family members almost always worried about job promotions, school grades, etc	T	F
56. Someone in our family played a musical instrument	T	F
57. Family members were not very involved in recreational activities outside work or school	T	F

58. We believed there were some things you should just have to take on faith	T	F
59. Family members made sure their rooms were neat	T	F
60. Every had an equal say in family decisions	T	F
61. There was very little group spirit in our family	T	F
62. Money and paying bills was openly talked about in our family	T	F
63. If there was a disagreement in our family, we tried hard to smooth things over and keep the peace	T	F
64. Family members strongly encouraged each other to stand up for their rights	T	F
65. In our family, we didn't try that hard to succeed	T	F
66. Family members often went to the library	T	F
67. Family members sometimes attended courses or took lessons for some hobby or interest (outside of school)	T	F
68. In our family each person had different ideas about what was right and wrong.	T	F
69. Each persons duties were clearly defined in our family	T	F
70. We could do whatever we wanted to in our family	T	F
71. We really got along well with each other	T	F
72. We were usually careful about what we said to eachother.	T	F
73. Family members often tried to one-up or out-do each other.	T	F
74. It was hard to be by yourself without hurting someone's feelings in our household	T	F

75. "Work before play" was the rule in our family.	T	F
76. Watching T.V. was more important than reading in our family.	T	F
77. Family members went out alot	T	F
78. The bible was a very important book in our home	T	F
79. Money was not handled very carefully in our family	T	F
80. Rules were pretty flexible in our family	T	F
81. There was plenty of time and attention for everyone in our family.	T	F
82. There were alot of spontaneous discussions in our family.	T	F
83. In our family, we believed you didn't get anywhere by raising your voice	T	F
84. We were not really encouraged to speak up for ourselves in our family.	T	F
85. Family members were often compared with others as to how well they were doing at work or school	T	F
86. Family members really liked music, art, and literature.	T	F
87. Our main form of entertainment was watching T.V. or listening to the radio.	T	F
88. Family members believed that if you sinned you would be punished.	T	F
89. Dishes were normally done immediately after eating	T	F
90. You couldn't get away with much in our family	T	F

NEO FIVE-FACTOR INVENTORY

Form S

Paul T Costa, Jnr., Ph.D., and Robert R McCrae, Ph.D

Instructions

Write only where indicated in the booklet. Carefully read all of the instructions before beginning.

This questionnaire contains 60 statements. Reach each statement carefully. For each statement tick the box for the response that best represents your opinion. Make sure that your answer is in the correct box.

Tick ***strongly disagree*** if you think that the statement is definitely false

Tick ***disagree*** if you think that the statement is mostly false

Tick ***neutral*** if you cannot decide, or the statement is about equally true and false

Tick ***agree*** if you think that the statement is mostly true

Tick ***strongly agree*** if you think that the statement is definitely true

For example, you would tick the ***strongly disagree*** box if you believe that a statement is definitely false:

Strongly disagree	Disagree	Neutral	Agree	Strongly agree
4				

Fill in only one response for each statement. Respond to all of the statements, making sure that you fill in the correct response.

Before responding to the statements, please enter your name, age and sex and the date at the top of the next page

Name..... Age..... Sex..... Date.....

	Strongly disagree	Disagree	Neutral	Agree	Strongly agree
1. I am not a worrier					
2. I like to have a lot of people around me					
3. I don't like to waste my time daydreaming					
4. I try to be courteous to everyone I meet					
5. I keep my belongings clean and neat					
6. I often feel inferior to others					
7. I laugh easily					
8. Once I find the right way to do something, I stick to it					
9. I often get into arguments with my family and co-workers					
10. I'm pretty good about pacing myself so as to get things done on time.					
11. When I'm under a great deal of stress, sometimes I feel like I'm going to pieces					
12. I don't consider myself especially "light-hearted"					
13. I am intrigued by the patterns I find in art and nature					
14. Some people think I'm selfish and egotistical					
15. I am not a very methodical person					
16. I rarely feel lonely or blue					
17. I really enjoy talking to people					
18. I believe letting students hear controversial speakers can only confuse and mislead them					

	Strongly disagree	Disagree	Neutral	Agree	Strongly agree
19 I would rather co-operate with others than compete with them					
20. I try to perform all the tasks assigned to me conscientiously					
21. I often feel tense and jittery					
22. I like to be where the action is					
23. Poetry has little or no effect on me					
21. I tend to be cynical and sceptical of others' intentions					
22. I have a clear set of goals and work towards them In an orderly fashion					
26. Sometimes I feel completely worthless					
27. I usually prefer to do things alone					
28. I often try new and foreign foods					
23. I believe that most people will take advantage of You if you let them					
30. I waste a lot of time before settling down to work					
31. I rarely feel fearful or anxious					
32. I often feel as if I am bursting with energy					
24. I seldom notice the moods or feelings that Different environments produce					
34. Most people I know like me					
35. I work hard to accomplish my goals					
36. I often get angry at the way people treat me					
37. I am a cheerful, high-spirited person					
25. I believe we should look to our religious Authorities for decisions on moral issues					
39. Some people think of me as cold and calculating					
40. When I make a commitment, I can always be counted on to follow through					

	Strongly disagree	Disagree	Neutral	Agree	Strongly agree
41. Too often, when things go wrong, I get Discouraged and feel like giving up					
42. I am not a cheerful optimist					
43. Sometimes when I am reading poetry or looking At a work of art, I feel a chill or wave of excitement					
42. I'm hard-headed and tough-minded in my attitudes					
43. Sometimes I'm not as dependable or reliable As I should be					
46. I am seldom sad or depressed					
47. My life is fast - paced					
44. I have little interest in speculating on the nature Of the universe or the human condition					
49. I generally try to be thoughtful and considerate					
50. I am a productive person who always gets the Job done					
45. I often feel helpless and want someone else to Solve my problems					
52. I am a very active person					
53. I have a lot of intellectual curiosity					
54. If I don't like people, I let them know it					
55. I never seem to be able to get organised					
46. At times I have been so ashamed, I just wanted To hide					
47. I would rather go my own way than be a leader Of others					
48. I often enjoy playing with theories or abstract ideas					
49. If necessary, I am willing to manipulate people to Get what I want					
60. I strive for excellence in everything I do					

THANK YOU FOR COMPLETING THIS QUESTIONNAIRE

Appendix V

RESEARCH INFORMATION SHEET

The Researcher (Fiona Simpson) is currently training in Clinical Psychology. She is required to undertake a research project as part of her Doctorate in Clinical Psychology. You have been asked to consider participating in this research.

The causes of Chronic Fatigue Syndrome (CFS) are currently not clearly understood. Many patients report that the onset of their illness followed a viral infection and often this is regarded as a cause. Other studies have demonstrated a strong association between CFS and emotional disorders and many believe that several different factors are involved in its causation. Some theories suggest that personality factors and family factors may in some cases, increase vulnerability to the development of CFS.

The study aims to explore family characteristics and personality dimensions in groups of individuals diagnosed with : Depression, Chronic Fatigue Syndrome, or both these disorders. You have been asked to participate because you are currently diagnosed with one of these illnesses.

As a subject you will be asked to complete four questionnaires. The first of these contains questions relating to aspects of your family of origin and is 90 items long. The second is a personality questionnaire, 60 items in length. The third is an assessment measure for depression and anxiety, consisting of 14 questions. The fourth is an assessment measure for Chronic Fatigue, consisting of 11 questions. Completion of these measures should take you approximately 30 minutes.

Participation in this research is entirely voluntary and you can take up to two weeks to think about it before you commit yourself. If you prefer not to participate, this will not affect your treatment, and you can change your mind at any point.

Strict confidentiality will apply to all information gathered and this will only be read by Fiona Simpson and your consultant.

If you would like to obtain further information about this study before making a decision about your participation, you can contact Dr Phillip Welsby at the Western General Hospital, tel-0131-537-2854.

If you decide to participate in this study, you will be given a copy of this information sheet and a copy of your signed consent form to keep.

Thank you for your time in considering this proposal.

INSTRUCTIONS FOR SUBJECTS

You are asked to complete the enclosed four questionnaires. You will probably find some of the questions difficult to answer within the response categories given i.e. yes/no or true/false. We appreciate this difficulty, but it is vitally important for the research that you respond to each question as best you can, choosing one of the response categories.

If you prefer you can make comments to supplement your responses, so long as you still choose one of the given response categories when answering the questions.

Thankyou for your efforts